Global Innovative ADC Market

Independent Market Research Report

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Frost & Sullivan
April 2025

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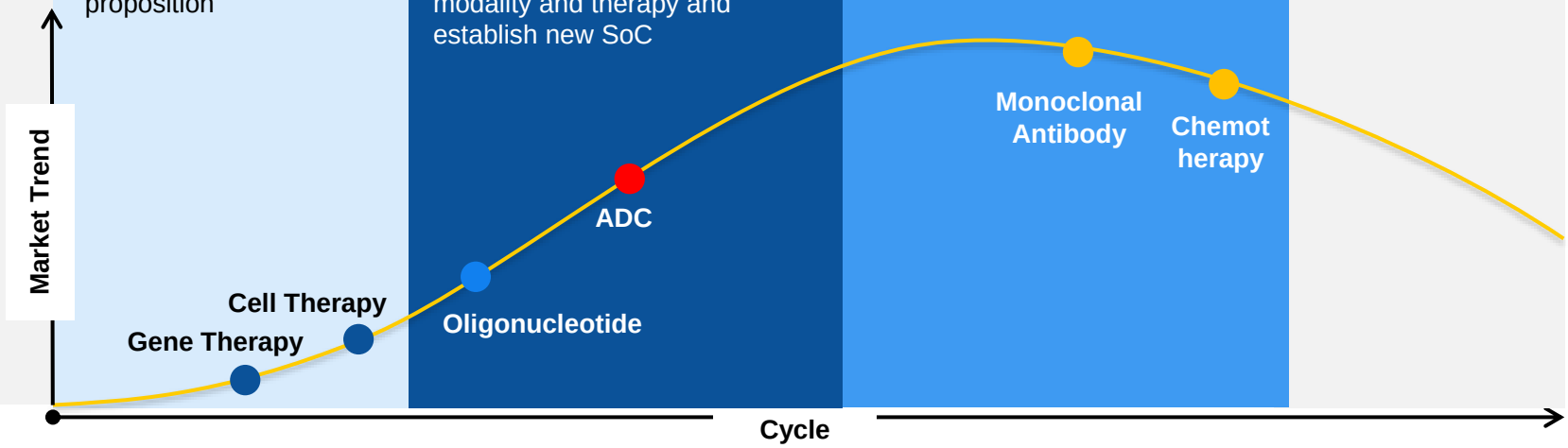
Development Path of Cancer Treatment

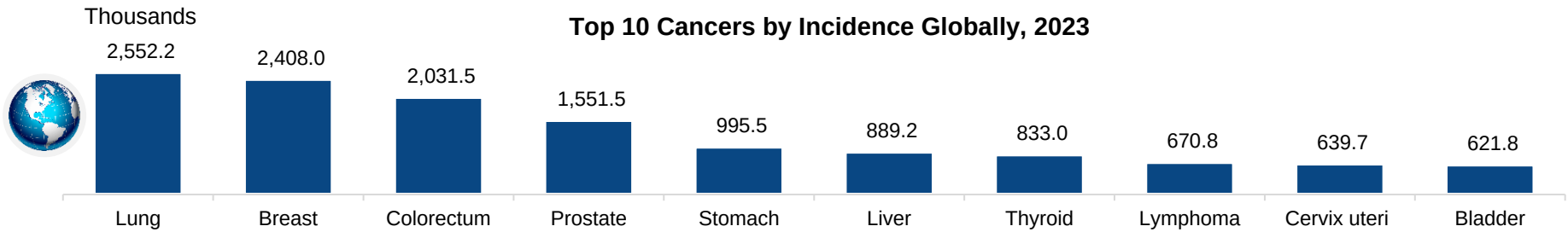
Development Stage	Emerging Stage	Rapid Growth Stage	Maturity Stage	Decline Stage
Market Environment	• Gaining awareness of the modality and therapy	• Increasing recognition and gaining attraction • Rapid adoption and market expansion	• Established recognition and widespread adoption	• Market saturation and demand decline
Industry Characteristics	• Few market competitions • Hypothesize, generate and test new ideas and technologies • Seek proof-of-concept on new indications • Explore and identify target market and market proposition	• Number of competitors increases and competitive landscape emerges • Seek differentiated strategies and product offerings • Growing investments drive innovations and breakthrough • Broaden the boundary of the modality and therapy and establish new SoC	• Market leaders emerge and begin to realize economies of scale • Major breakthroughs or disruptions are less common • Focus on broadening clinical application and market penetration	• Market growth stabilizes • Reduction in product categories and number of competitors

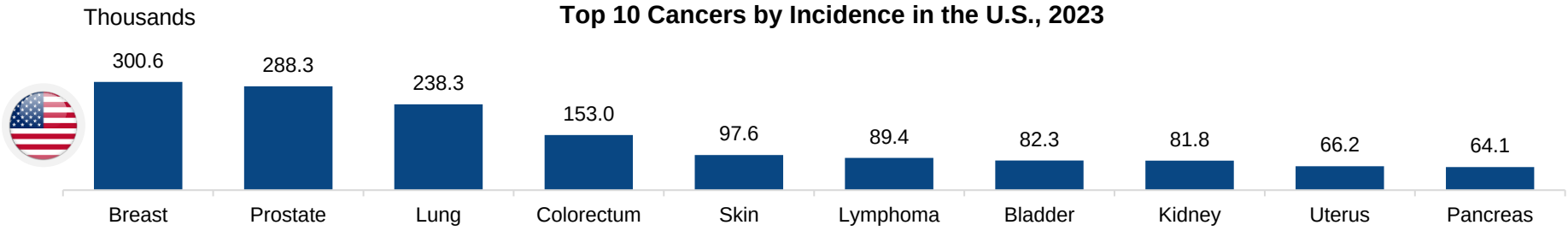


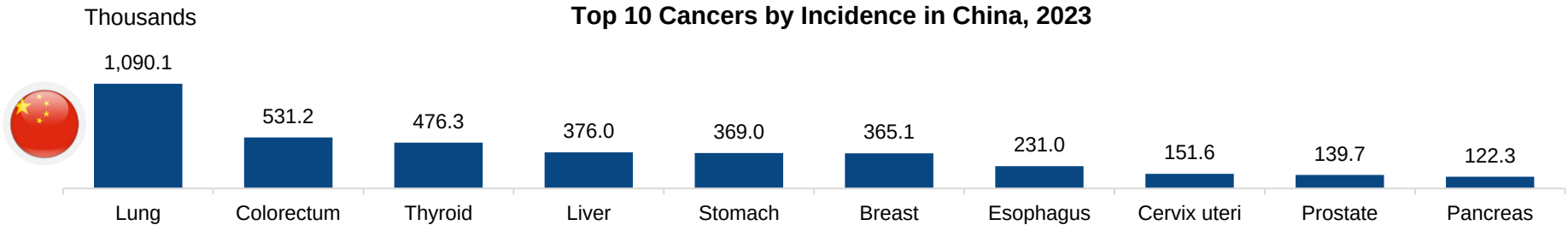
Source: Literature review, Frost & Sullivan Analysis

Top 10 Cancers by Incidence, 2023

- The top 5 cancers by incidence globally in 2023 are lung cancer, breast cancer, colorectal cancer, prostate cancer and stomach cancer.
- The increasing smoking population are the risk factors of lung cancer in China. And the higher incidence of stomach and colorectal cancer are associated with unhealthy diet, eating habits and manner in China.







Note: Head and neck cancer is a collective term for cancers that occur in various parts of the head and neck, so it is not included in the ranking of single cancer incidence.

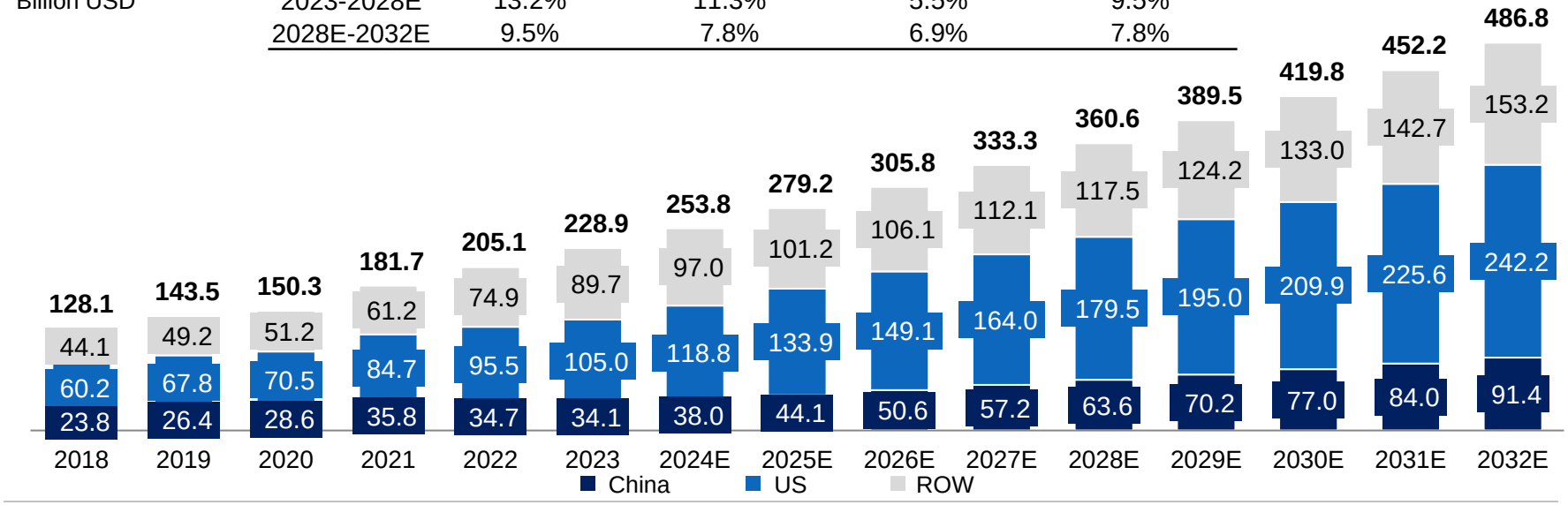
Source: Globocan, IARC, NCCR, Frost & Sullivan analysis

Global Cancer Drug Market, 2018-2032E

- From 2018 to 2023, global cancer market expanded from USD 128.1 billion to USD 228.9 billion, representing a CAGR of 12.3% during this period. Global cancer market is expected to reach USD 486.8 billion by 2032, representing a CAGR of 7.8% from 2028 to 2032.
- The U.S. cancer market has grown from USD 60.2 billion in 2018 to USD 105.0 billion in 2023, with a CAGR of 11.8%. It is expected to reach USD 179.5 billion in 2028 and further increase to USD 242.2 billion in 2032, with a CAGR of 11.3% and 7.8% respectively.
- From 2023 to 2028, the Chinese cancer market is anticipated to grow from USD 34.1 billion to USD 63.6 billion, with a CAGR of 13.2%. It is estimated to achieve USD 91.4 billion in 2032, with a CAGR of 9.5% from 2028 to 2032.

Global Cancer Drug Market, 2018-2032E

Period	CAGR			
	China	U.S.	ROW	Global
2018-2023	7.5%	11.8%	15.2%	12.3%
2023-2028E	13.2%	11.3%	5.5%	9.5%
2028E-2032E	9.5%	7.8%	6.9%	7.8%



Source:Frost & Sullivan Analysis

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Analysis of Treatment Methods for Auto-immune Disease

Type	Subtype	Mechanism of Action	Representative Drugs	Dates of Market Launch	Drawbacks
Anti-inflammatory Agents	NSAIDs	Exert an anti-inflammatory effect by inhibiting the activity of cyclooxygenase (COX)	Aspirin	1899	• Traditional non-selective NSAIDs inhibit platelet aggregation and cause significant gastrointestinal disorders such as bleeding, ulcers, and perforation
			Ibuprofen	1969	
	SAIDs (Glucocorticoids)	Prevent the formation of both PGs and LTs by causing the release of lipocortin, which by inhibition of phospholipase A2 reduces arachidonic acid release	Prednisone	1955	• Long-term GC use should be individualized based on patient characteristics and minimized due to their potential AEs
			Dexamethasone	1958	
Targeted Biologics	Anti-TNF Antibodies	Bind to TNF-α to prevent its association with receptors on the cell surface, thereby blocking the signaling pathways mediated by TNF-α	Infliximab	1998	• May affect the normal immune function and its response, leading to the development of many autoimmune phenomena and diseases • May affect the normal immune function and its response, leading to the development of many autoimmune phenomena and diseases • Long-term use of targeted biologics can easily lead to the drug resistance, thereby reducing the therapeutic effect • Inconvenience of intravenous administration, leading to poor patient compliance
			Adalimumab	2002	
			Etanercept	1998	
			Rilonacept	2008	
	Interleukin Related Drugs	Target and inhibit interleukins involved in inflammation	Anakinra	2001	
			Secukinumab	2015	
	Other Monoclonal Antibodies	Target specific antigens on cells (e.g., CD20, CD22), leading to cell lysis or inhibition of cell proliferation	Rituximab	1997	
			Ocrelizumab	2017	
Other Novel Therapy	CAR-T	Modify the patients' T-cells to recognize and attack abnormal B-cells	Under development	N.A.	• Side effects are potentially severe or even life-threatening immune-related toxicities, specifically cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) • Long manufacturing time and high treatment costs

Note: The CAR-T product has not yet been approved for indications in autoimmune diseases

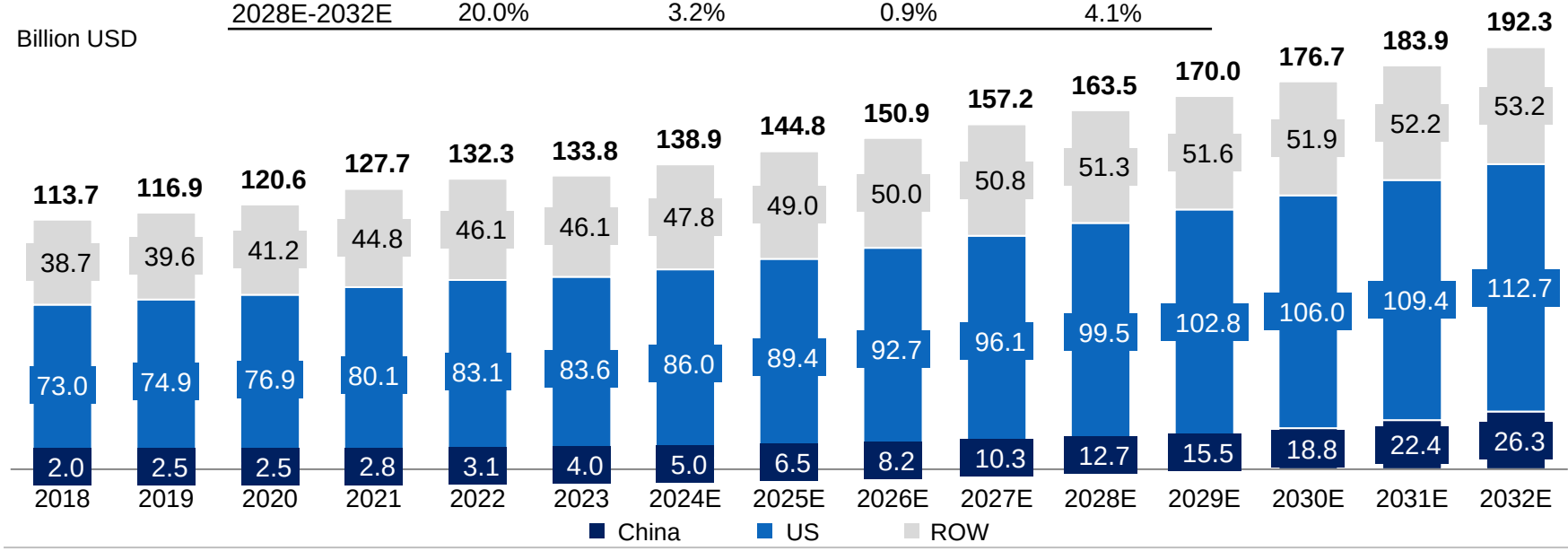
Source: Literature Review, Frost & Sullivan Analysis

Global Autoimmune Disease Drug Market, 2018-2032E

- The global autoimmune disease drug market size is expected to grow from USD 133.8 billion in 2023 to USD 163.5 billion in 2028 with a CAGR of 4.1%.
- The U.S. autoimmune disease drug market has grown from USD 73.0 billion in 2018 to USD 83.6 billion in 2023, with a CAGR of 2.8%. It is expected to reach USD 112.7 billion in 2032, with a CAGR of 3.2% from 2028 to 2032.
- Based on China's huge population, there is a large patient pool in the Chinese market. The Chinese autoimmune disease drug market is expected to reach USD 12.7 billion in 2028, representing a CAGR of 27.3% from 2023.

Global Autoimmune Disease Drug Market, 2018-2032E

Period	CAGR			
	China	U.S.	ROW	Global
2018-2023	13.4%	2.8%	3.7%	3.3%
2023-2028E	27.3%	3.5%	2.1%	4.1%
2028E-2032E	20.0%	3.2%	0.9%	4.1%



Source: Frost & Sullivan Analysis

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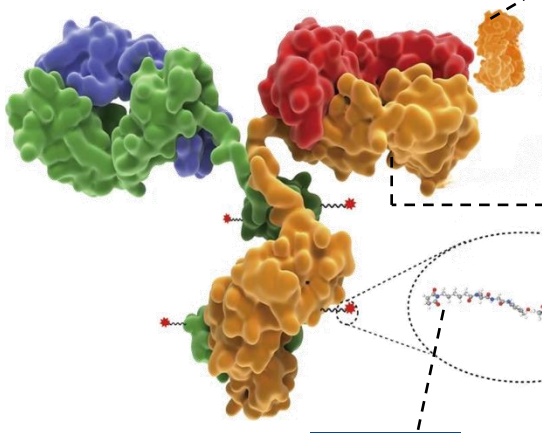
Overview of Antibody-Drug Conjugate (ADC) Therapy

- ADCs are complex molecules composed of an antibody linked to a biologically active (anticancer) agent. ADC targets a specific antigen only found on target cells. Once it binds to the cell, it triggers internalization of the antibody, together with the drug, thus killing the cancer cell. This maximizes efficacy and minimizes systemic exposure. The main structure and mechanism of action of ADC are elaborated below.

Main Structure of ADC



Target Antigen

Recognition of target cancer cell

Antibody

Guidance system for cytotoxic drugs

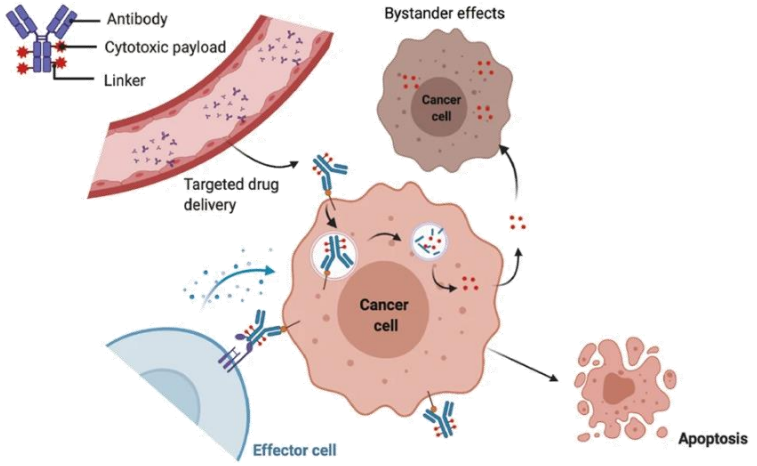
Linker

Bridge between antibody and drugs and to control the releasee of drugs inside cancer cell

Cytotoxic drug

Warhead for destroying cancer cell

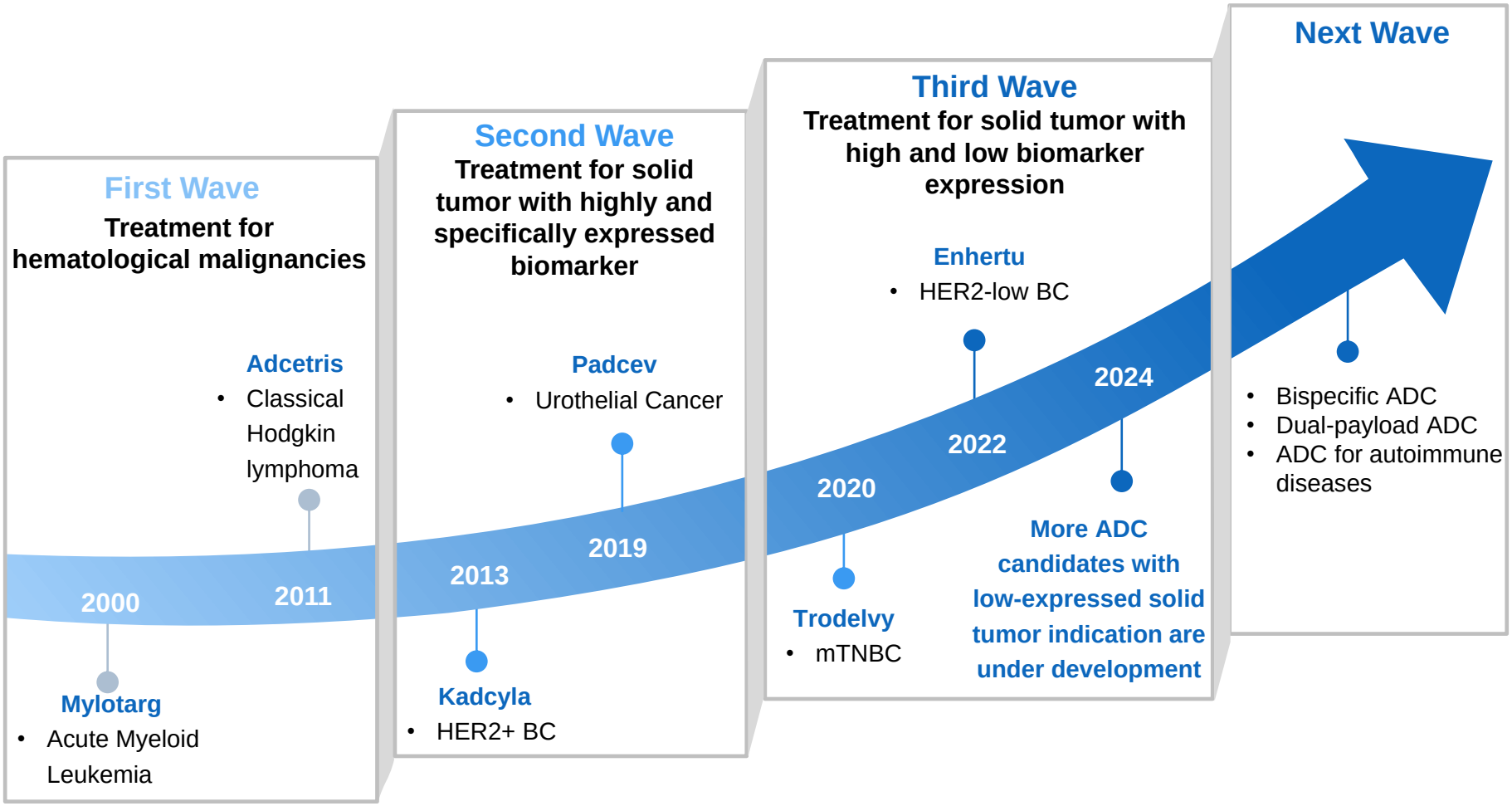
Mechanism of Action of ADC



- Once mAb of ADC is bound to the target antigens that specifically expressed on the cancer cells, the ADC is endocytosed/internalized by cells to form an early endosome, followed a maturation into late endosomes and finally fused with lysosomes.
- The cytotoxic payloads are eventually via either chemical or enzyme mediated release in the lysosomes, resulting in cell apoptosis or death via targeting DNA or microtubules.
- When the payload released is permeable or transmembrane, it may also induce bystander effect to enhance the efficacy of ADC.

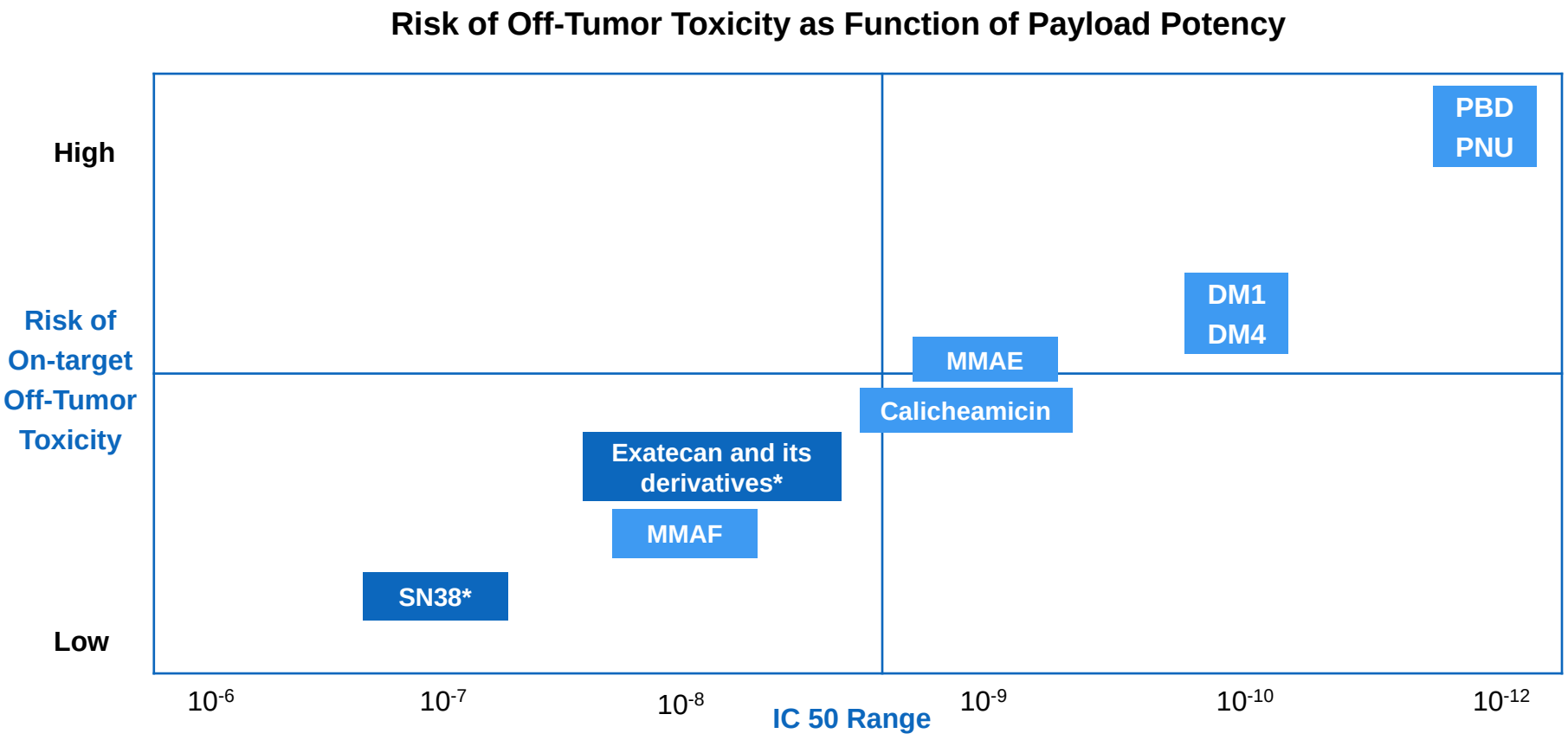
Source: Antibody drug conjugate: the "biological missile" for targeted cancer therapy, Frost & Sullivan Analysis

Three Waves of ADCs



Source: FDA, NMPA, Frost & Sullivan Analysis

Risk of Off-Tumor Toxicity as Function of Payload Potency



Note:* Topoisomerase-based payload

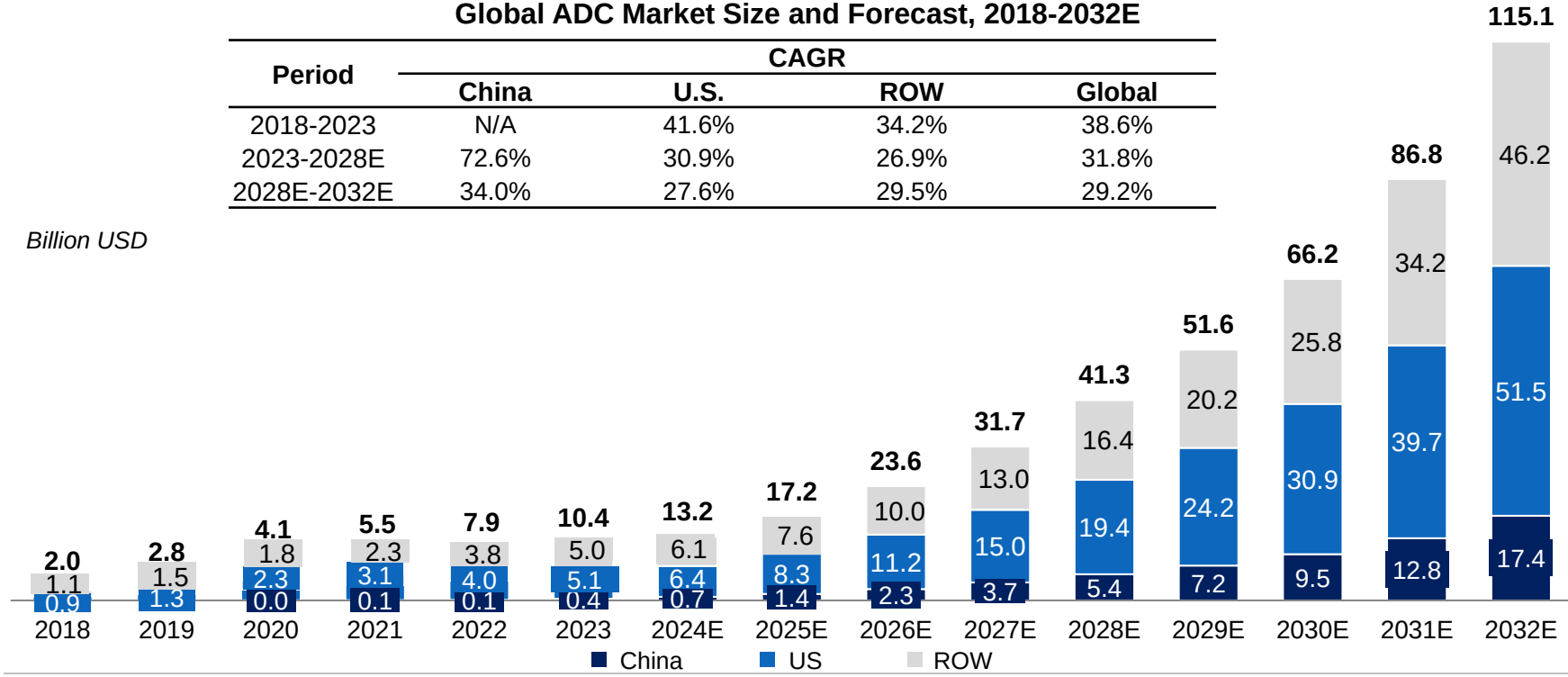
Source: ENA 2022, Frost & Sullivan Analysis

Global ADC Market Size and Forecast, 2018-2032E

- The global ADC market has grown rapidly in the past few years, from USD 2.0 billion in 2018 to USD 10.4 billion in 2023, with a CAGR of 38.6%. It is expected to reach USD 41.3 billion in 2028, with a CAGR of 31.8% from 2023 to 2028, and further increase to USD 115.1 billion in 2032, with a CAGR of 29.2% from 2028 to 2032.
- The U.S. ADC market has grown from USD 0.9 billion in 2018 to USD 5.1 billion in 2023, with a CAGR of 41.6%. It is expected to reach USD 19.4 billion in 2028 and further increase to USD 51.5 billion in 2032, with a CAGR of 30.9% and 27.6% respectively.
- From 2023 to 2028, the Chinese ADC market is anticipated to grow from USD 0.4 billion to USD 5.4 billion, with a CAGR of 72.6%, which is much faster than that of the global market. It is estimated to achieve USD 17.4 billion in 2032, with a CAGR of 34.0% from 2028 to 2032.

Global ADC Market Size and Forecast, 2018-2032E

Period	CAGR			
	China	U.S.	ROW	Global
2018-2023	N/A	41.6%	34.2%	38.6%
2023-2028E	72.6%	30.9%	26.9%	31.8%
2028E-2032E	34.0%	27.6%	29.5%	29.2%



Source: Frost & Sullivan Analysis

Growth Drivers of ADCs Drug Market

Expanding patient base with unmet needs	• The global cancer incidence reached 20.8 million cases in 2023, and is projected to increase to 25.5 million cases in 2032.Incidence is growing in major tumor types currently covered by approved ADCs, including certain subtypes of BC and non-small cell lung cancer (“NSCLC”). Other cancers, such as EC, ovarian cancer (“OC”), small-cell lung cancer (“SCLC”) and castration-resistant prostate cancer (“CRPC”), are also growing in global incidence. Due to the lack of effective treatments, as well as the occurrence of drug resistance and relapse, the five-year survival rate for cancer remains low, highlighting the demand for novel therapies to improve cancer prognosis and outcome. Notably, ADCs have emerged as a promising upgrade to chemotherapy in cancer treatment, as they combine the specificity of antibodies with the potent cell-killing ability of cytotoxic drugs, representing a significant market opportunity.
Broadened application through technology advances	• Significant investments are being devoted to cancer research and drug development, with the goal to further elucidate disease biology and discover targeted cancer treatments that improve patient outcomes. In particular, ongoing ADC research and development on novel payloads can potentially yield new designs that improve the therapeutic effects of this modality and reduce toxicity that limits the use of some marketed ADCs. To date, there are over 100 ADC candidates under clinical development globally targeting new indications not covered by approved ADCs. These efforts will drive ADCs towards becoming a backbone cancer therapy and their expansion into other therapeutic areas.
Dynamic collaboration among market players	• There has been a surge of collaboration and licensing deals in the ADC industry, with large MNCs increasing investments into this field and smaller biotechnology companies contributing significantly to the R&D of ADC candidates. Biotechnology companies often leverage their innovative capabilities and expertise to conduct initial exploratory work and proof-of-concept studies, while collaborating with MNCs provides substantial technical, financial and regulatory support to expedite further development and commercialization of promising ADC candidates. Meanwhile, in-licensing components for innovative drug development has emerged as a common practice, especially for complex therapeutics like ADCs. The enhanced collaboration among biotechnology companies to advance the R&D and commercialization of ADCs also contributes substantially to the growth of the ADC market. For example, in June 2024, MabCare Therapeutics entered into a license agreement with Day One Biopharma for a PTK7 ADC candidate. In December 2024, our Company entered into a collaboration and license agreement with Avenzo regarding the R&D and commercialization of an EGFR/HER3 BsADC candidate. Overall, synergistic collaboration models have become increasingly instrumental in bringing novel candidates to the market.

Source: Frost & Sullivan analysis

Future Trends of ADCs Drug Market

Novel payloads and linkers	• Although traditional payloads have been proven to be effective, there is a growing focus on exploring novel payloads to expand the range of treatable cancer types and overcome drug resistance, as more patients are treated with, and acquire resistance to, existing ADCs. In addition, beyond the site-specific conjugation methods of existing ADCs, researchers are exploring more sophisticated linker designs aimed to further improve payload delivery and release while reducing off-target toxicity.
Wider coverage of targets and expression levels	• Expression level refers to the quantity of specific targets present on the surface of cells. Many solid tumors express low or heterogeneous levels of targets, limiting the applicability of existing ADCs that focus on tumors with high expression levels of targets. Research is underway to develop ADC candidates effective against solid tumors with low expression. For example, recent advancements in ADC design, including the development of topoisomerase-based payloads, have resulted in successful applications of HER2 ADCs for HER2-low BC patients. Novel targets such as HER3 and B7-H3 have also emerged, drawing significant industry attention. Research into these emerging targets aims to broaden the landscape of tumor antigens that can be leveraged for the selective delivery of cytotoxic payloads.
Novel ADC formats	• New formats such as bispecific and multi-specific ADCs are a rising trend in the development of next-generation ADCs. Compared to monospecific ADCs, BsADCs can potentially target and kill tumor cells more precisely by simultaneously targeting two different antigens to overcome tumor heterogenicity, and reduce the risk of off-target toxicity. Some BsADCs can also harness the patient's own immune system through simultaneous immune-modulation to achieve synergistic anti-tumor effects. Moreover, BsADCs can potentially overcome drug resistance to monospecific ADCs by blocking escape pathways, making them more promising for extended duration of response.

Source: Frost & Sullivan analysis

Future Trends of ADCs Drug Market

Expansion to non-oncology therapeutic areas	• With technological advances in progress, ADCs are expected to cover a wider range of cancer types as well as expand to non-oncology areas such as autoimmune, metabolic and cardiovascular diseases. With the ability to minimize off-target effects and systemic toxicity through targeting specificity, ADCs have become a promising option for these chronic, non-oncology conditions that require treatments with improved safety profiles. This expansion is likely to bring new market potential for ADCs in the near future.
Combination with other treatment modalities and expansion of treatment lines	• The mechanism of action of ADCs is highly synergistic with other treatment modalities to potentiate tumor cell killing. Combination strategies have shown to be crucial in improving efficacy and promising as first-line treatments for a broader patient population. Notably, a strong biological rationale supports the investigation of combining ADCs with IO to overcome the occurrence of resistance and improve treatment outcomes for cancer patients. ADCs interact with cancer cells and immune cells through mechanisms such as immunogenic cell death, antibody-dependent cell mediated cytotoxicity and dendritic cell activation, leading to synergistic effects when combined with IO therapies such as immune checkpoint inhibitors (“ICIs”). Combination therapies of ADCs with tyrosine kinase inhibitors (“TKIs”) have also shown promise in clinical studies to enhance anti-tumor efficacy..

Source: Frost & Sullivan analysis

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HER2 Expressions and Potential Indications

- Human epidermal growth factor receptor 2 (HER2) is a member of the epidermal growth factor receptor family having tyrosine kinase activity. Dimerization of the receptor results in the autophosphorylation of tyrosine residues within the cytoplasmic domain of the receptors and initiates a variety of signaling pathways leading to cell proliferation and tumorigenesis.
- HER2 overexpression or mutation is widely recognized as a major driver of some of the most prevalent cancers, including BC, NSCLC and GC. HER2 overexpression has also been seen in other cancers like ovary, endometrium, bladder, lung, colon, and head and neck. HER2-low expression was frequent across a broad spectrum of solid tumors, such as BC, OC and EC.

Cancer	HER2+ (IHC 3+ or IHC 2+ /ISH +)	HER2 – Low (IHC 2+/ISH- or IHC 1+)
Breast cancer	15–30%	45-55%
Gastric cancer	9–38%	30-35%
Colorectal cancer	5-6%	45-50%
Ovarian Cancer	20-30%	60-70%
Esophageal Cancer	7-22%	N/A
Endometrial Cancer	17–30%	47-53%
NSCLC	7-23%	N/A

Source: Literature Review, Frost & Sullivan Analysis

Global Marketed HER2-ADCs

Drugs	Company	Target	Payload	Linker	Indication	Treatment Line	FDA Approval	NMPA Approval	Price	NRDL inclusion	U.S. Insurance/Assistance Program Coverage
Kadcyla® (Adotrastuzumab emtansine; T-DM1)	Roche	HER-2	DM1	SMCC (Non-cleavable)	HER2+ BC	≥2L	2013.02	2021.06	US$4,148/100mg	Yes	100%
					HER2+ EBC	Adjuvant	2019.05	2020.01			
Enhertu® (Trastuzumab deruxtecan; DS8201)	Daiichi Sankyo /AstraZeneca	HER-2	DXD	Glycine-glycine-phenylalanine-glycine (Cleavable)	HER2+ BC	≥3L	2019.12	N/A	US$2,967/100mg	No	100%
					HER2+ GC or GJA	≥2L	2021.01	2024.08			
					HER2+		2022.05	2023.02			
					HER2-low BC		2022.08	2023.07			
					HER2m NSCLC						
					HER2+ solid tumors		2022.08	N/A			
							2024.04	N/A			
					HR-positive, HER2-low or HER2-ultralow BC		2025.01	N/A			
Aidixi (Disitamab Vedotin; RC48)	RemeGen	HER-2	MMAE	Valine-Citrulline (Cleavable)	HER2-overexpression GC	≥3L	N/A	2021.06	RMB 3,800/60mg	Yes	N/A
					HER2-overexpression UC	≥2L		2022.01			

By March 28th. 2025

Note: 1. Price of Aidixi is the price after medical insurance ;

2. RemeGen didn't disclose the sales revenue of Aidixi;

3. With the Genentech Oncology® Co-pay Assistance Program, eligible patients with commercial insurance could pay as little as $0 per treatment for KADCYLA;

4. Eligible patients with a valid prescription of ENHERTU may pay as little as $0 per infusion and $0 out-of-pocket costs for ENHERTU through Patient Assistance Programs.

Source: FDA, NMPA, Drug.com, Annual Report, Frost & Sullivan

Competitive Landscape of MRCT HER-2 ADC Trials

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
DS-8201	NSCLC Harboring HER2 Exon 19 or 20 Mutations	Phase 3	Daiichi Sankyo /AstraZeneca	2021-09-17	Global
	Biliary Tract Cancer	Phase 3		2024-06-21	Global
	HER2-low or HER2 null BC	Phase 3		2024-09-27	Global
	HER2+, pMMR EC	Phase 3		2024-11-05	Global
	HER2-Overexpressing CRC	Phase 2		2021-02-09	Global
	HER2-Expressing tumors, incl. EC	Phase 2		2020-07-22	Global
DB-1303/BNT323	HR+/HER2-low BC	Phase 3	DualityBio /BioNTech	2023-08-30	Global
	HER2- Expressing EC	Phase 3		2024-04-01	Global
SYD985	HER2+ BC	NDA*	Byondis	2022-07-18	Global
	HER2- Expressing EC	Phase 2		2019-12-19	Global
ARX788	HER2+ BC	Phase 2	Ambrx/NovoCodex	HER2+ BC	Global
RC48	HER2-Expressing UC	Phase 2	RemeGen/Seagen	2021-05-10	Global
	HER2-Expressing Solid Tumors，incl. EC	Phase 2		2023-08-21	Global
DX126-262	HER2+ BC	Phase 2	DAC Biotech	2021-08-10	Global

By March 28th. 2025

Note: only incl. MRCT trials ≥ phase 2; Global means ≥ 3 countries;

In 2023.5, FDA issued a complete response letter to SYD985 which requested additional information that will require additional time and resources that extend beyond the current evaluation period.

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Competitive Landscape of non-MRCT HER-2 ADC Trials (1/3)

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
A166	HER2+ BC	NDA	Kelun-Biotech	2023-05-11	China
DS-8201	GC	NDA	Daiichi Sankyo/AstraZeneca	2023-12-12	China
	NSCLC	NDA		2024-02-08	China
	HER2-overexpressing solid tumors	Phase 2		2024-03-08	China
DB-1303	HER2+ BC	Phase 3	DualityBio /BioNTech	2023-11	China
RC48	HER2-low BC	Phase 3	RemeGen	2020-05-11	China
	GC With HER2-overexpression	Phase 3		2021-01-19	China
	HER2-Expressing UC	Phase 3		2022-03-31	China
	HER2+ BC	Phase 2/3		2018-04-18	China
	HER2-overexpressing BTC	Phase 2		2020-04-01	China
	HER2-expressing Gynecological Malignancies	Phase 2		2021-07-16	China
	Muscle-Invasive Bladder Cancer	Phase 2		2022-03-28	China
	Cervical Cancer	Phase 2		2023-12-04	China
SHR-A1811	HER2+ BC	Phase 3	Hengrui Pharmaceuticals	2022-06-16	China
	HER2-low BC	Phase 3		2023-04-12	China
	HER2+ GC or GJA	Phase 3		2023-11-08	China
	CRC	Phase 3		2023-12-27	China
	HER2-Mutated NSCLC	Phase 3		2024-05-22	China
	Epithelial ovarian, fallopian tube, or primary peritoneal cancer	Phase 3		2025-02-14	China
	HER2+ BTC	Phase 2		2025-02-13	China

By March 28th. 2025

Note: only incl. non-MRCT trials ≥ phase 2 ; incl. the trials in clinical trials and CDE with the location in China

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Competitive Landscape of non-MRCT HER-2 ADC Trials (2/3)

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
MRG002	HER2+ UC	Phase 3	Miracogen	2023-01-29	China
	HER2+ BC	Phase 2/3		2021-05-31	China
	HER2-low BC	Phase 2		2021-02-22	China
	HER2+/HER2-low GC or GJA	Phase 2		2021-11-01	China
FS-1502	HER2+ BC	Phase 3	Fosun Pharmaceutical	2023-02-27	China
	NSCLC	Phase 2		2022-01-18	China
	RAS/BRAF wild-type HER2+ CRC	Phase 2		2022-01-30	China
	HER2-Expressing GC	Phase 2		2022-09-01	China
DP303c	HER2+ BC	Phase 3	CSPC Group	2023-06-12	China
	HER2-Expressing OC	Phase 2		2021-03-29	China
	HER2-Expressing GC	Phase 2		2021-04-01	China
JSKN003	HER2-low BC	Phase 3	Alphamab	2023-10-07	China
	Platinum-resistant Relapsed Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	Phase 3		2024-12-27	China
	HER2+ BC	Phase 3		2025-02-05	China
DB-1303/BNT323	HER2+ BC	Phase 3	DualityBio /BioNTech	2023-11-29	China
BL-M07D1	HER2+ BC	Phase 3	Baili Pharm	2024-03-14	China
	HER2+ GC or GJA	Phase 2		2024-05-21	China
TQB2102	HER2-low BC	Phase 3	Chia Tai Tianqing	2024-08-19	China
	HER2+ BC	Phase 2		2024-01-10	China
	HER2-IHC 0 BC	Phase 2		2024-03-25	China
	HER2- BC	Phase 2		2024-06-11	China
	HER2 Gene Abnormality NSCLC	Phase 2		2024-07-11	China
	HER2+ gastroesophageal adenocarcinoma	Phase 2		2024-10-29	China
	advanced gynaecological tumour	Phase 2		2025-02-13	China

By March 28th. 2025

Note: only incl. non-MRCT trials ≥ phase 2 ; incl. the trials in clinical trials and CDE with the location in China

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Competitive Landscape of non-MRCT HER-2 ADC Trials (3/3)

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
GQ1005	HER2+ BC	Phase 3	GeneQuantum	2024-12-24	China
IBI354	Platinum-resistant Relapsed Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	Phase 3	Innovent	2025-02-06	China
ARX788	HER2+ BC	Phase 2/3	Ambrx/NovoCodex	2020-06-30	China
	HER2+ GC or GJA	Phase 2/3		2021-06-29	China
BB-1701	HER2-Mutated NSCLC	Phase 2	Eisai/Bliss Biopharmaceutical	2023-11-02	China
	HER2+ or HER2-low BC	Phase 2		2024-01-03	U.S., Japan
	HER2-Expressing or HER2-Mutated Solid Tumors	Phase 2		2024-09-26	China
FDA022-BB05	HER2- expressing EC, HER2-low BC and HER2-overexpressing solid tumor	Phase 2	Shanghai Fudan-Zhangjiang	2024-04-23	China
SHR-4602	HER2-Expressing or HER2-Mutated Solid Tumors	Phase 2	Hengrui Pharmaceuticals	2024-07-24	China

By March 28th. 2025

Note: only incl. non-MRCT trials ≥ phase 2 ; incl. the trials in clinical trials and CDE with the location in China

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Overview of Breast Cancer

- Breast cancer is a disease in which abnormal breast cells grow out of control and form tumors. It is is the most common cancers in women and mostly happens in women aged 50.
- With the increasing importance of driver genes, breast cancer can be divided into four subtypes according to whether the patient has gene mutation, hormone receptor, and cellular molecular status: LuminalA, LuminalB, HER-2 overexpression type, and triple-negative type (Basal-like type).

Risk Factors

- Genetic predisposition(BRCA1 or BRCA2 mutations)
- Estrogen and progesterone exposure
- Oral contraceptives or birth control drugs
- Atypical hyperplasia of the breast
- Lobular carcinoma in situ
- Lifestyle factors(weight, food, alcohol, physical activity)
- Breast density(dense breast tissue)
- Family history of breast cancer

Molecular Subtypes

Subtypes/ Indicators	HER-2	ER	PR	Ki-67
HER-2 positive (HR negative)	+	-	-	Any
HER-2 positive (HR positive)	+	+	Any	Any
Triple-negative	-	-	-	Any
Luminal A	-	+	+ and high expression	<14%
Luminal B (HER-2 negative)	-	+	low expression or -	high expression

Classification of HER-2 Expression		
HER-2 Positive	IHC 3+ or IHC 2+ and ISH positive	
HER-2 Negative	HER-2 low expression	IHC 2+ and ISH negative or IHC 1+
	HER-2 IHC 0	IHC 0

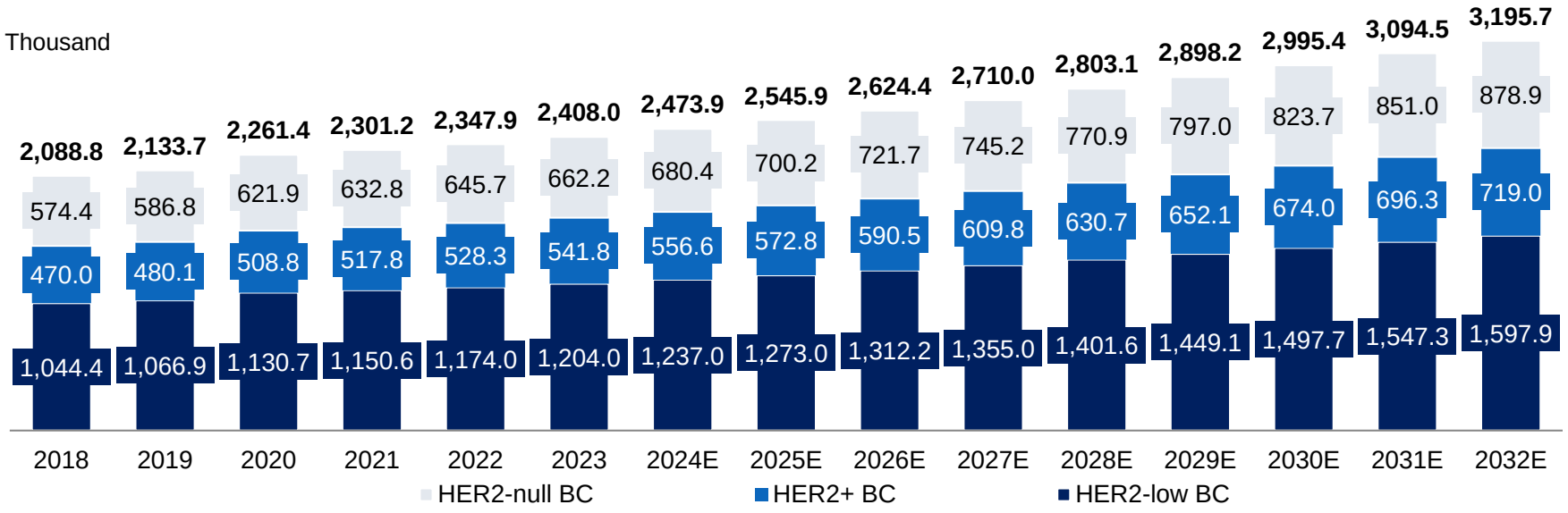
Source: Literature Review, Frost & Sullivan Analysis

Incidence of Breast Cancer in Global, 2018-2032E

- The incidence of HER2-low and HER2-positive BC is predicted to rise globally from 1,044.4 and 470.0 thousand cases in 2018 to 1,597.9 and 719.0 thousand cases by 2032.
- The overall incidence of BC cases worldwide rose from 2,088.8 thousand in 2018 to 2,408.0 thousand in 2023, with a CAGR of 2.9%, and is projected to reach 2,803.1 thousand by 2028 and 3,195.7 thousand by 2032.

Incidence of Breast Cancer in Global, 2018-2032E

	CAGR			
	HER2-null BC	HER2-low BC	HER2+ BC	Total
2018-2023	2.9%	2.9%	2.9%	2.9%
2023-2028E	3.1%	3.1%	3.1%	3.1%
2028E-2032E	3.3%	3.3%	3.3%	3.3%



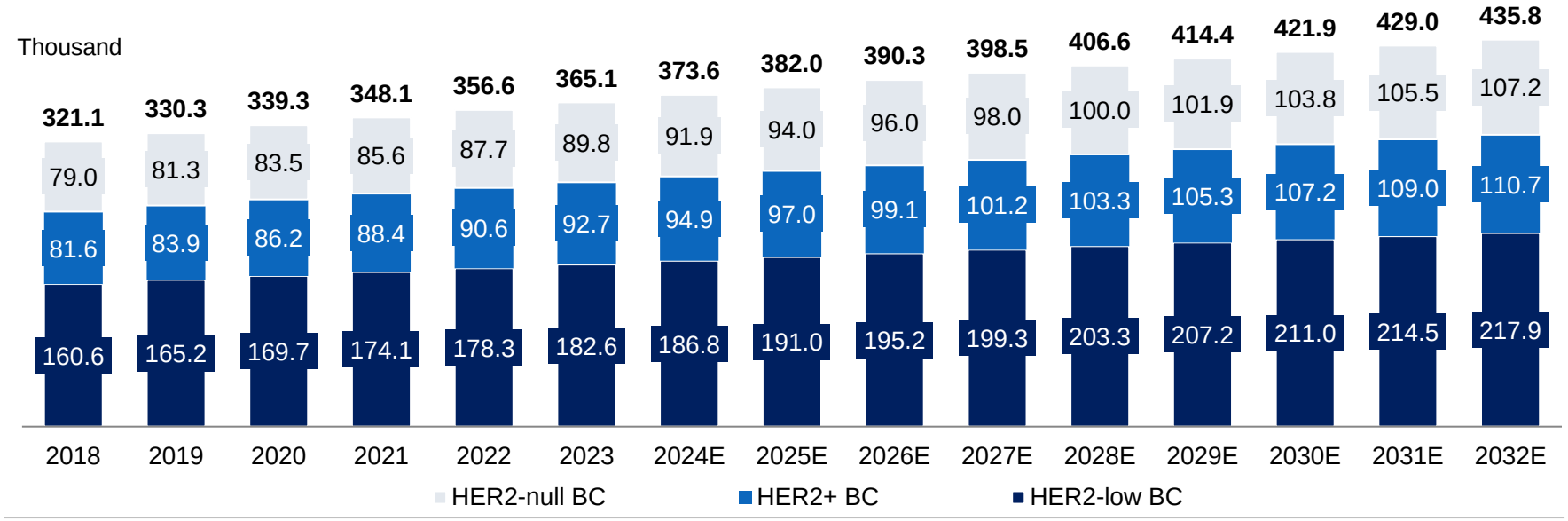
Source: Frost & Sullivan analysis

Incidence of Breast Cancer in China, 2018-2032E

- In China, HER2-low and HER2-positive BC cases are projected to rise from 160.6 thousand and 81.6 thousand in 2018 to 217.9 thousand and 110.7 thousand by 2032, accounting for about 75.4% of total BC.
- Total BC cases incidence in China increased from 321.1 thousand in 2018 to 365.1 thousand in 2023, with a CAGR of 2.6%, and is projected to reach 406.6 thousand by 2028 and 435.8 thousand by 2032.

Incidence of Breast Cancer in China, 2018-2032E

	CAGR			
	HER2-null BC	HER2-low BC	HER2+ BC	Total
2018-2023	2.6%	2.6%	2.6%	2.6%
2023-2028E	2.2%	2.2%	2.2%	2.2%
2028E-2032E	1.7%	1.7%	1.7%	1.7%



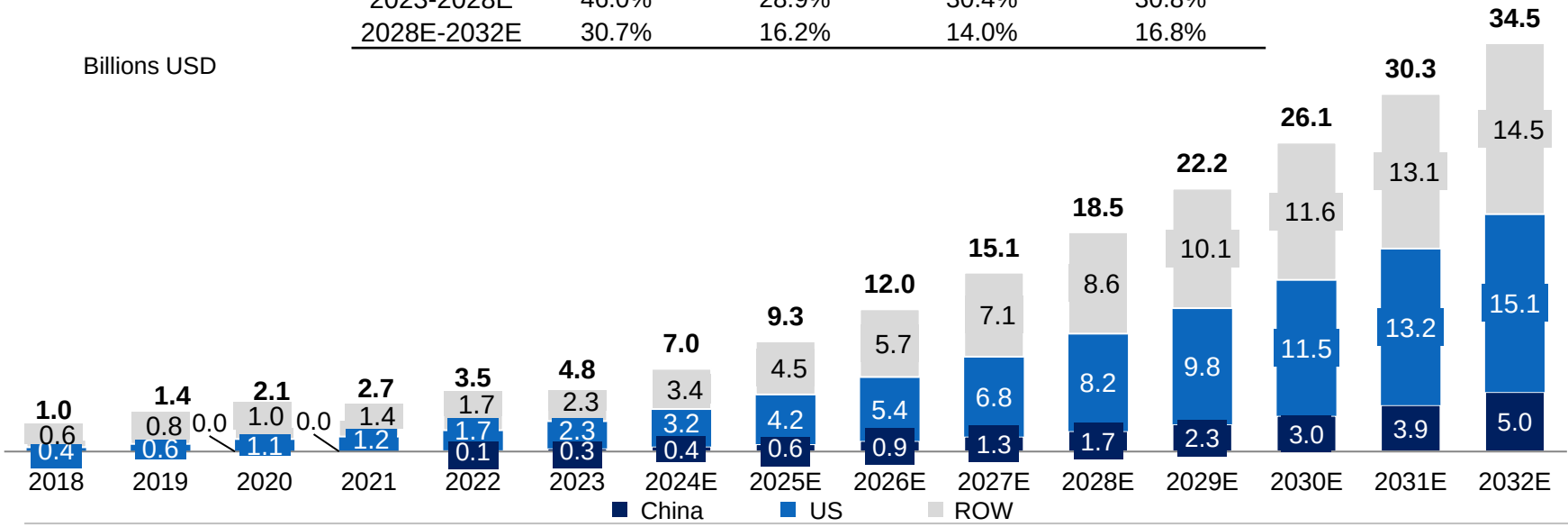
Source: Frost & Sullivan analysis

Global HER2 ADCs Market Size, 2018-2032E

- Global HER2 ADCs market is estimated to increase from USD 4.8 billion in 2023 to 18.5 billion in 2028, with a CAGR of 30.8%. In the future, the global HER2 ADCs market will further increase to USD 34.5 billion in 2032, with a CAGR of 16.8% from 2028 to 2032.
- The U.S HER2 ADCs market is estimated to increase from USD 1.7 billion in 2023 to 6.8 billion in 2028, with a CAGR of 28.9%. It will further increase to USD 15.1 billion in 2032, with a CAGR of 16.2% from 2028 to 2032.
- Until 2020, the first ADC targeting HER2 was approved for marketing in China. It is the beginning for nationally developed ADC drugs. HER2 ADCs market in China reached USD 0.3 billion in 2023Chinese HER2 ADCs market will further increase to USD 5.0 billion in 2032.

Global HER2 ADCs Market Size, 2018-2032E

Period	CAGR			
	China	US	ROW	Global
2018-2023	NA	44.5%	29.1%	37.1%
2023-2028E	46.0%	28.9%	30.4%	30.8%
2028E-2032E	30.7%	16.2%	14.0%	16.8%



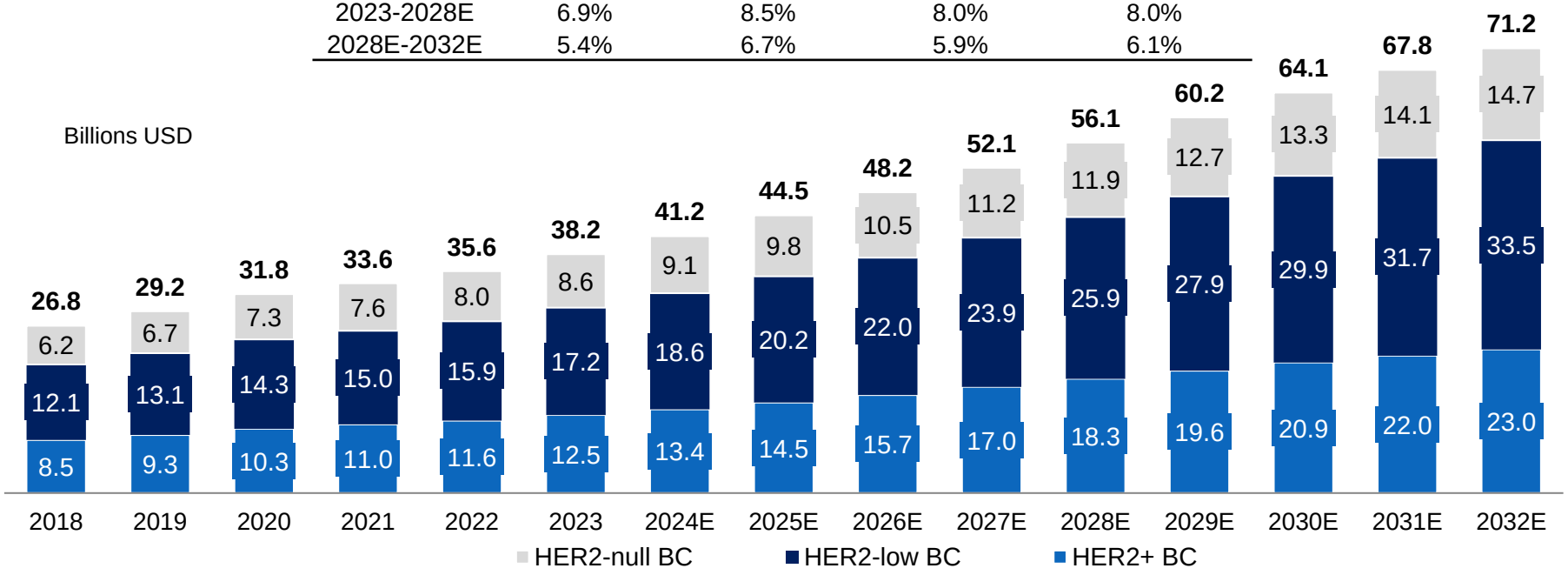
Source: Frost & Sullivan analysis

Global Breast Cancer Drug Market Size, 2018-2032E

- Global breast cancer drug market is estimated to increase from USD 38.2 billion in 2023 to 56.1 billion in 2028, with a CAGR of 8.0%. In the future, the global breast cancer drug market will further increase to USD 71.2 billion in 2032, with a CAGR of 6.1% from 2028 to 2032.
- The global HER2-low breast cancer patient treatment drug market size reached USD 17.2 billion in 2023, with a CAGR of 7.3% from 2018 to 2023. The market size is expected to reach USD 25.9 billion in 2028, with a CAGR of 8.5% from 2023 to 2028. The market will further grow to USD 33.5 billion in 2032, with a CAGR of 6.7% from 2028 to 2032.

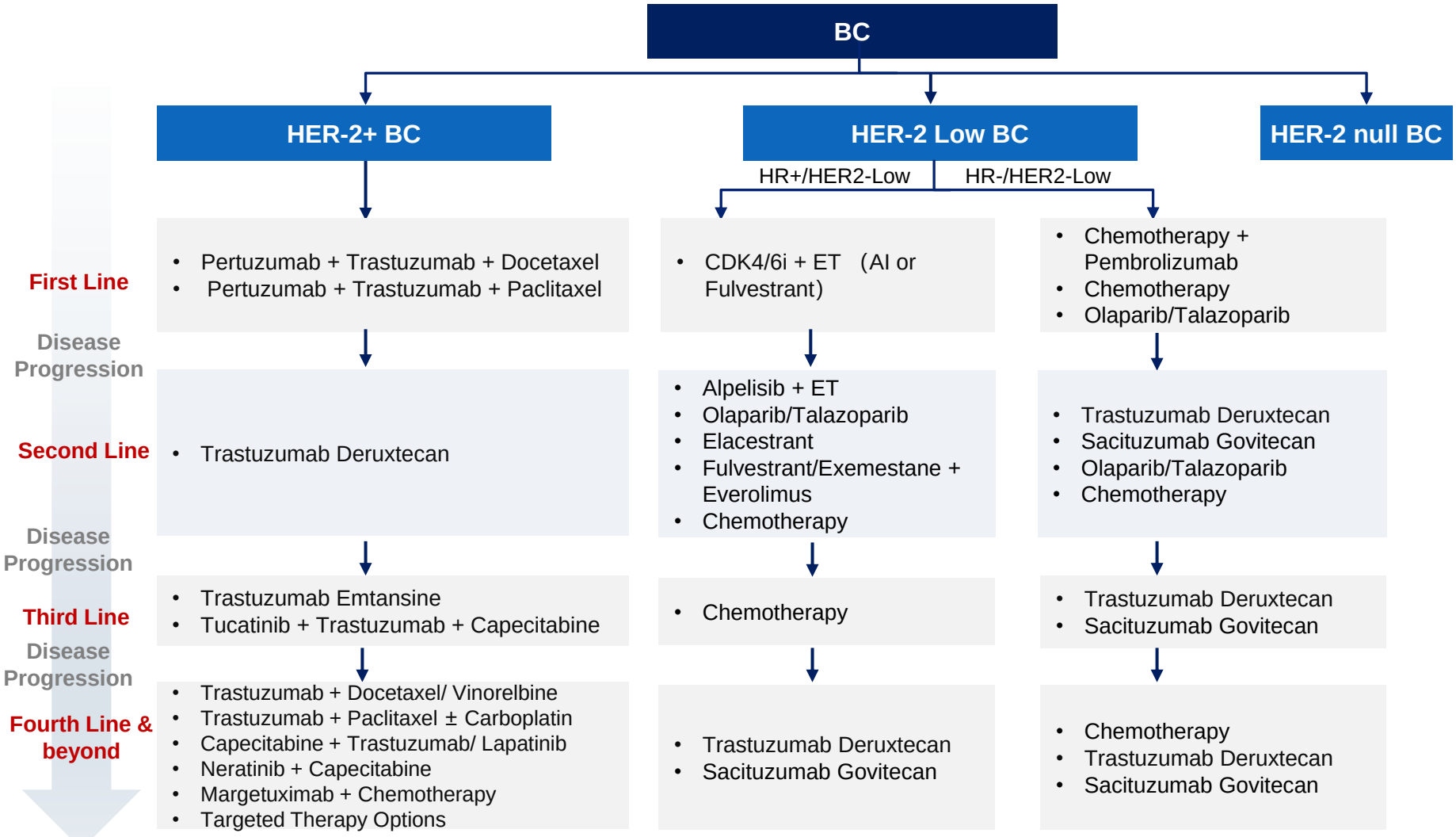
Global Breast Cancer Drug Market Size, 2018-2032E

Period	CAGR			
	HER2-null BC	HER2-low BC	HER2+ BC	Total
2018-2023	6.6%	7.3%	8.0%	7.4%
2023-2028E	6.9%	8.5%	8.0%	8.0%
2028E-2032E	5.4%	6.7%	5.9%	6.1%



Source: Frost & Sullivan analysis

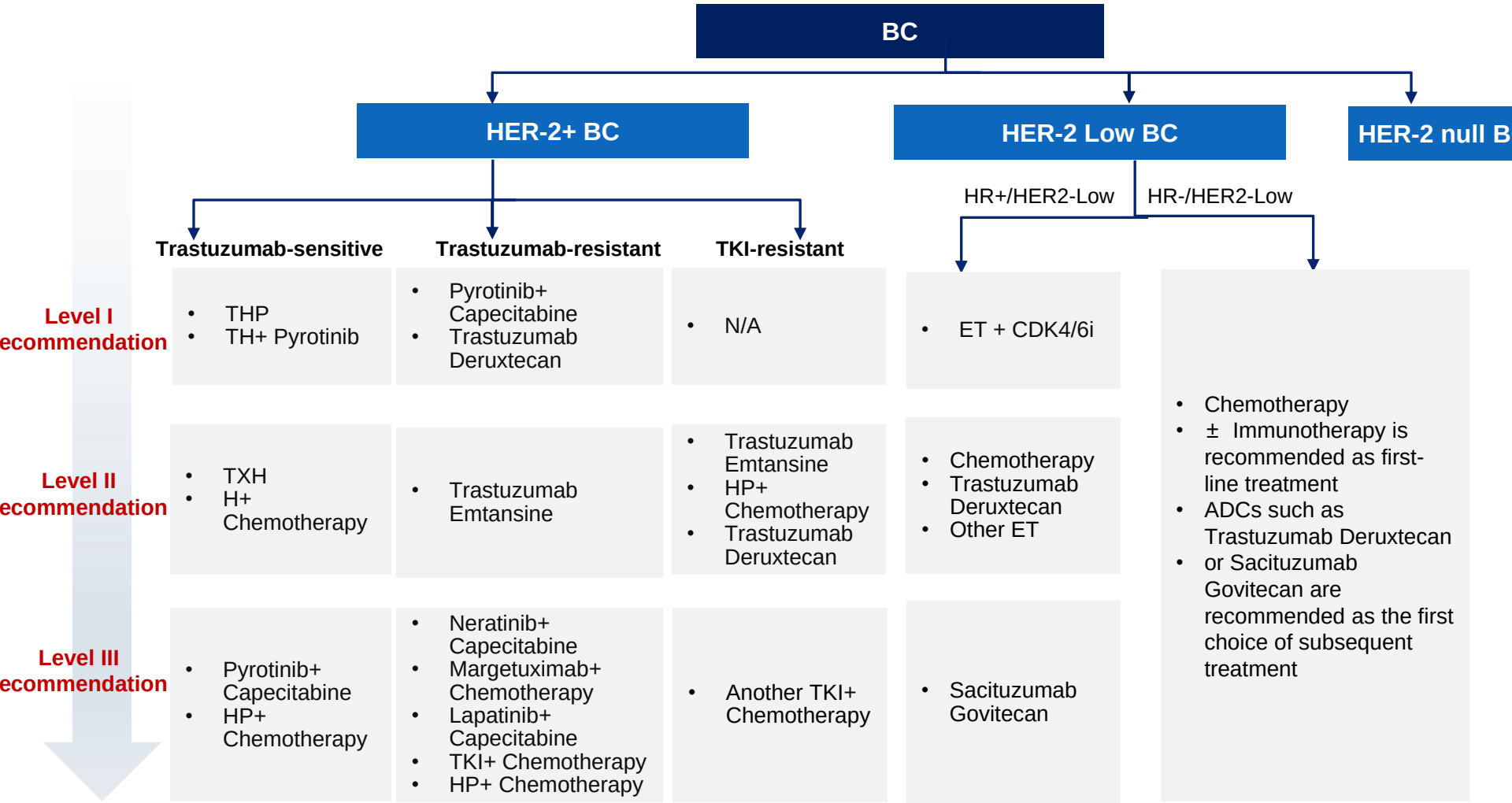
Treatment Paradigm of HER-2+ and HER2-Low BC in U.S.



Notes: CDK4/6 i=Cyclin-dependent Kinase 4 and 6 Inhibitors; ET=Endocrine Therapy; DB-1303 is indicated for 1L HER2+ BC and chemo naïve HER2-low BC patients in U.S.; DB-1310 is indicated for post-Enhertu HER2+ BC patients.

Source: NCCN 2024, A review of treatment options in HER2-low breast cancer and proposed treatment sequencing algorithm, Frost & Sullivan Analysis

Treatment Paradigm of HER-2+ and HER2-Low BC in China



Notes: THP=Taxanes combined with trastuzumab and pertuzumab; TH= Taxanes combined with trastuzumab, H= trastuzumab; TXH= docetaxel and trastuzumab plus capecitabine; CDK4/6 i=Cyclin-dependent Kinase 4 and 6 Inhibitors; ET=Endocrine Therapy; DB-1303 is indicated for HER2+ BC and chemo naïve HER2-low BC patients in China; DB-1310 is indicated for post-Enhertu HER2+ BC patients.

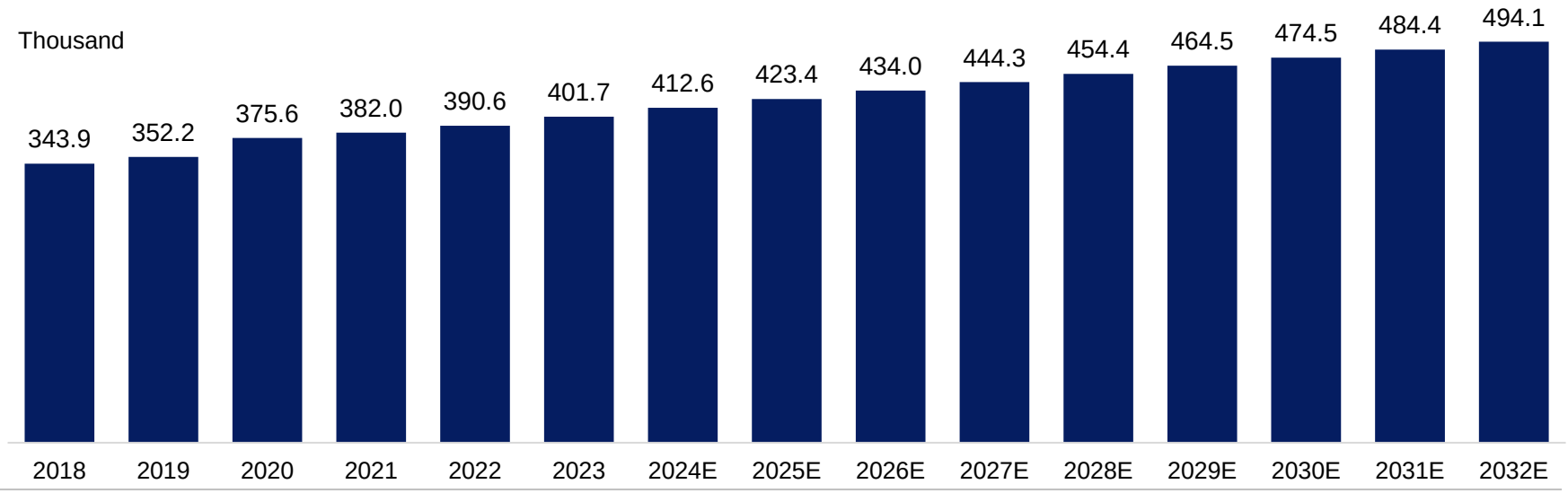
Source: CSCO 2024, Frost & Sullivan Analysis

Incidence of Endometrial Cancer in Global, 2018-2032E

- The incidence of endometrial cancer globally increased from 343.9 thousand cases in 2018 to 401.7 thousand cases in 2023, with a CAGR of 3.2%. According to projections, the incidence will increase to 454.4 thousand cases by 2028, representing a 2.5% CAGR. By 2032, it is expected to reach 494.1 thousand cases, with a CAGR of 2.1%.

Incidence of Endometrial Cancer in Global 2018-2032E

	CAGR
2018-2023	3.2%
2023-2028E	2.5%
2028E-2032E	2.1%



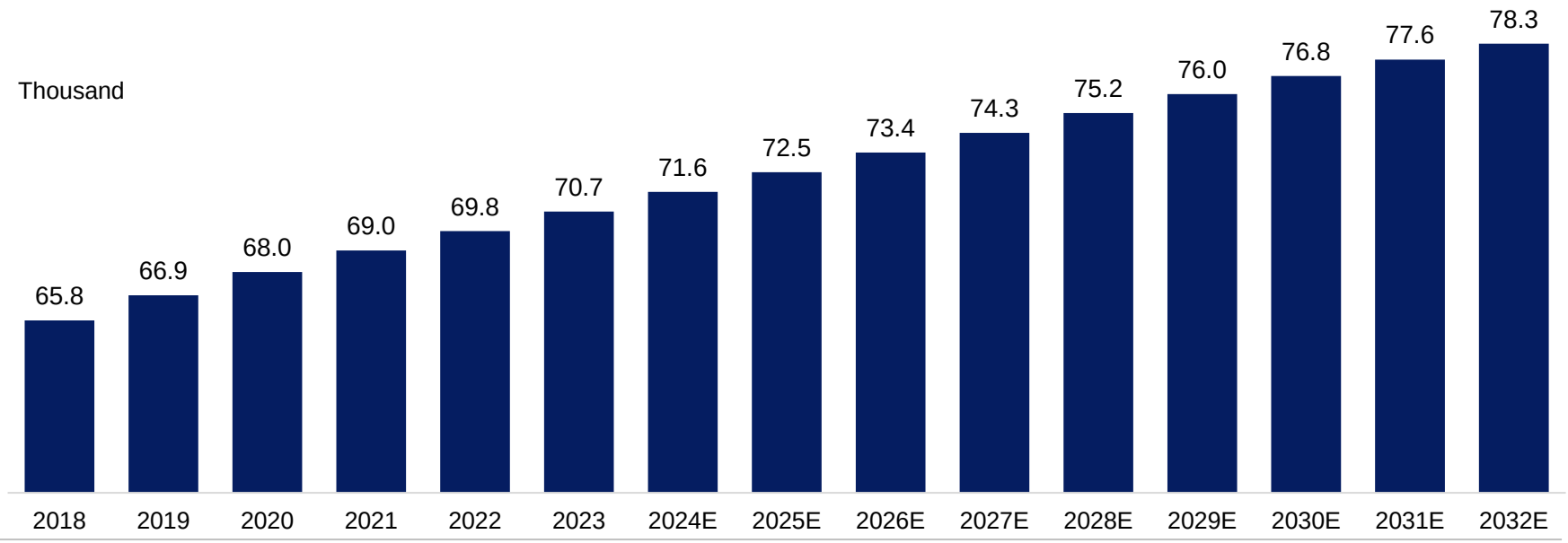
Source: Frost & Sullivan analysis

Incidence of Endometrial Cancer in China, 2018-2032E

- The incidence of endometrial cancer in China grew from 65.8 thousand cases in 2018 to 70.7 thousand cases in 2023, representing a CAGR of 1.5%. Forecasts indicate that the number of cases will increase to 75.2 thousand by 2028, with a CAGR of 1.2%. By 2032, the incidence is expected to reach 78.3 thousand cases, showing a CAGR of 1.0%.

Incidence of Endometrial Cancer in China 2018-2032E

	CAGR
2018-2023	1.5%
2023-2028E	1.2%
2028E-2032E	1.0%



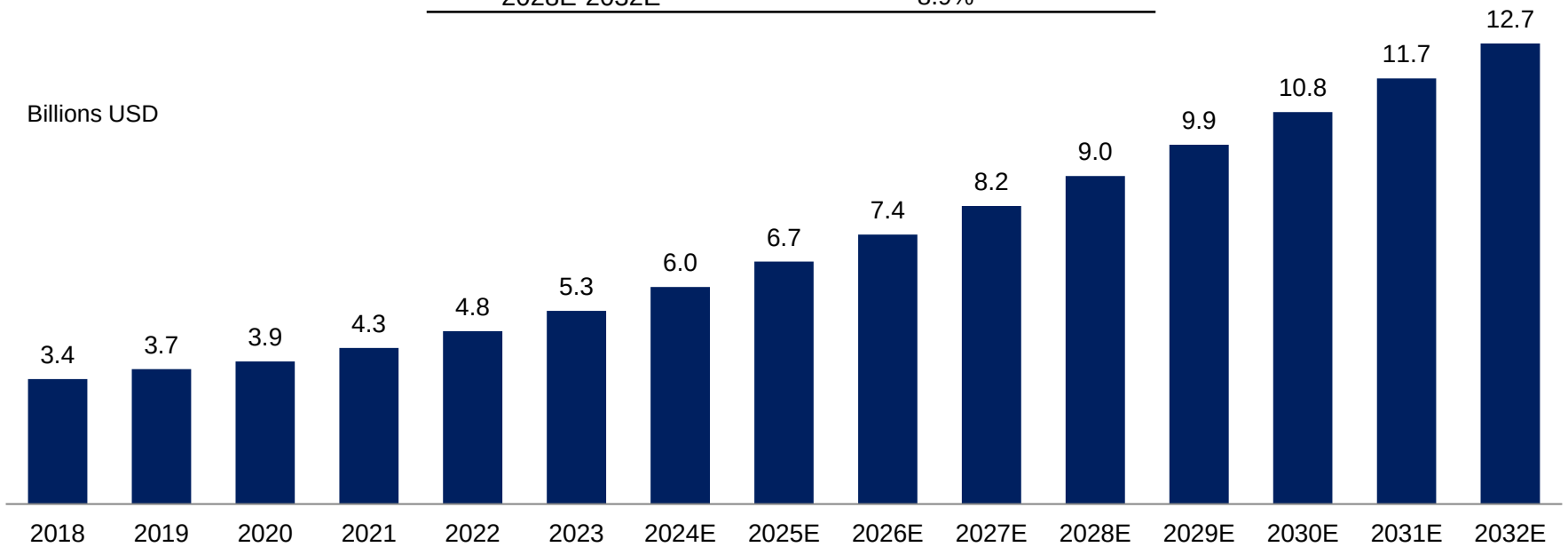
Source: Frost & Sullivan analysis

Global Endometrial Cancer Drug Market Size, 2018-2032E

- Global endometrial cancer drug market is estimated to increase from USD 5.3 billion in 2023 to 9.0 billion in 2028, with a CAGR of 11.2%. In the future, the global endometrial cancer drug market will further increase to USD 12.7 billion in 2032, with a CAGR of 8.9% from 2028 to 2032.

Global Endometrial Cancer Drug Market Size, 2018-2032E

Period	CAGR
2018-2023	9.1%
2023-2028E	11.2%
2028E-2032E	8.9%



Source: Frost & Sullivan analysis

B7H3 Expressions and Potential Indications

- B7-H3, also known as CD276, is a co-stimulatory/inhibitory molecule of the B7 family. It can promote T cell activation and IFN-γ production. B7-H3 has an inhibitory effect in adaptive immunity, such as inhibiting T cell priming, proliferation and the release of effector cytokines (mainly IFN-γ and IL-2), inhibiting the activity of NK cells, etc.
- B7-H3 protein is highly expressed in a variety of malignant tumors, including cervical cancer, pancreatic cancer, lung cancer, gastric cancer, osteosarcoma, ovarian cancer, etc.

Cancer	B7H3 Expression Ratio
Breast Cancer	57-74%
Gastric Cancer	58%
Hepatocellular Carcinoma	92%
NSCLC	74%
SCLC	65%
CRPC	93%

Source: Literature Review, Frost & Sullivan Analysis

Competitive Landscape of MRCT B7H3 ADC Trials

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
DS-7300	SCLC	Phase 3	Daiichi Sankyo/Merck Sharp & Dohme	2024-01-12	Global
	ESCC	Phase 3		2025-02-19	Global
MGC018	mCRPC and Other Solid Tumors, incl. SCLC	Phase 2	MacroGenics	2022-09-22	Global
DB-1311/BNT324	Solid Tumors, incl. SCLC,CRPC and other cancers	Phase 1/2	DualityBio/BioNTech	2023-06-22	Global
	Advanced Lung Cancer	Phase 1/2		2025-03-25	Global
HS-20093/GSK5764227	Gastrointestinal Solid Tumors	Phase 1/2	Shanghai Hansoh./GlaxoSmithKline	2025-03-25	Global
	Solid Tumors	Phase 1		2024-08-13	Global
YL201	Solid Tumors	Phase 1	MediLink.	2022-09-23	U.S., China
BGB-C354	Solid Tumors	Phase 1	BeiGene	2024-10-14	Global

By March 28th. 2025

Note: Global means ≥ 3 countries; Trial about MGC018 on mCRPC patients was suspended according to MacroGenics announcement dated 2024/7/30

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Competitive Landscape of non-MRCT B7H3 ADC Trials

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
DS-7300	Solid Tumors, incl. EC, CRC	Phase 2	Daiichi Sankyo/Merck Sharp & Dohme	2024-03-26	U.S.
	Solid Tumors, incl. SCLC, CRPC	Phase 1/2		2019-10-30	U.S., Japan
HS-20093/GSK5764227	Limited-stage SCLC	Phase 3	Shanghai Hansoh/GlaxoSmith Kline	2024-07-30	China
	Osteosarcoma and Other Sarcomas	Phase 2		2023-03-28	China
	mCRPC	Phase 2		2023-08-21	China
	HNSCC	Phase 2		2023-08-23	China
	Extensive-Stage SCLC	Phase 2		2023-09-25	China
	Esophageal Carcinoma	Phase 2		2023-11-01	China
	Solid Tumors	Phase 1		2022-03-11	China
	Bone and soft tissue sarcomas	Phase 1		2024-12-05	China
YL201	SCLC	Phase 3	MediLink.	2024-11-24	China
	mCRPC	Phase 2		2024-01-26	China
	Solid Tumors, incl. SCLC	Phase 1/2		2023-08-29	China
MHB088C	Solid Tumors, incl. SCLC, CRPC	Phase 1/2	Minghui Pharmaceutical	2022-12-15	Australia
7MW3711	Solid Tumors	Phase 1/2	Mabwell	2023-08-10	China
IBI129	Solid Tumors, incl. SCLC	Phase 1/2	Innovent	2023-08-14	Australia

By March 28th. 2025

Note: Global means ≥ 3 countries; Trial about MGC018 on mCRPC patients was suspended according to MacroGenics announcement dated 2024/7/30

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Competitive Landscape of non-MRCT B7H3 ADC Trials

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
ILB-3101	Solid Tumors, incl. SCLC	Phase 1/2	Innolake Biopharm	2024-05-23	China
MGC018	Solid Tumors, incl. CRPC	Phase 1	MacroGenics	2022-03-24	U.S.
BAT8009	Solid Tumors	Phase 1	Bio-Thera	2022-06-06	China
MGC026	Solid Tumors, incl. SCLC	Phase 1	MacroGenics	2024-02-05	U.S., Australia
BGB-C354	Solid Tumors	Phase 1	BeiGene	2024-05-21	U.S., Australia
SYS6043	Solid Tumors, incl. SCLC	Phase 1	CSPC Group	2024-12-27	China
BB-1712	Solid Tumors	Phase 1	Bliss Biopharmaceutical	2025-01-22	China

By March 28th. 2025

Note: Global means ≥ 3 countries; Trial about MGC018 on mCRPC patients was suspended according to MacroGenics announcement dated 2024/7/30

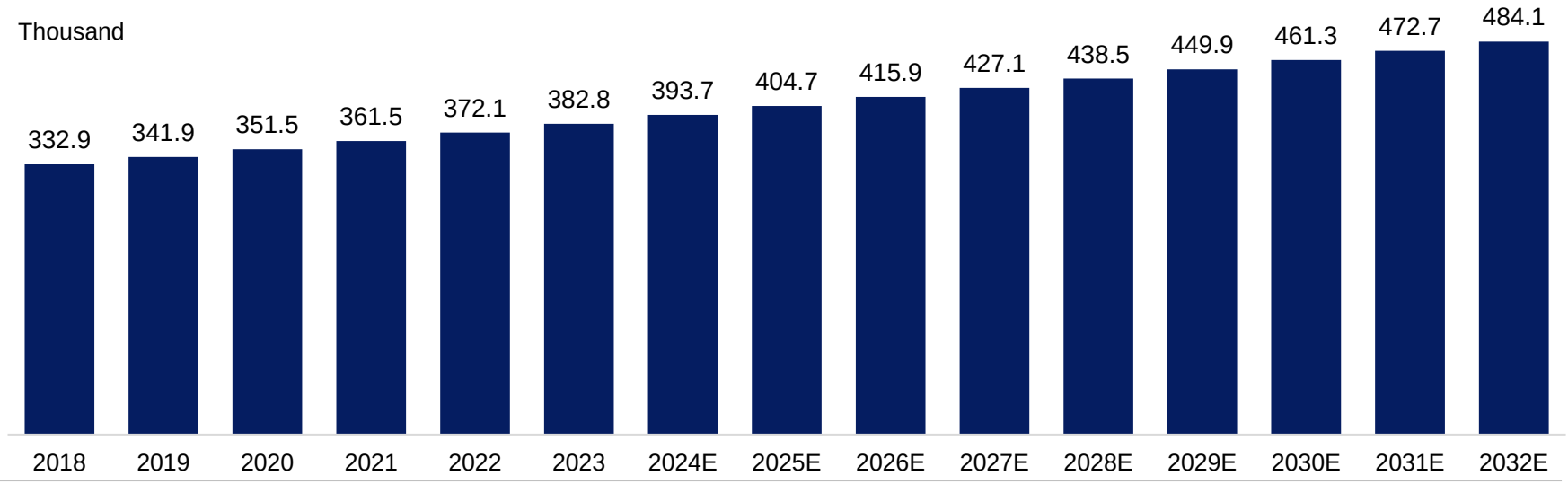
Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Incidence of SCLC in Global, 2018-2032E

- The global incidence of SCLC rose from 332.9 thousand cases in 2018 to 382.8 thousand cases by 2023, demonstrating an CAGR of 2.8%. Forecasts indicate that by 2028, the number of cases will increase to 438.5 thousand, maintaining a similar growth rate of 2.8%. By 2032, the incidence is expected to reach 484.1 thousand cases, with CAGR of 2.5%.

Incidence of SCLC in Global 2018-2032E

	CAGR
2018-2023	2.8%
2023-2028E	2.8%
2028E-2032E	2.5%



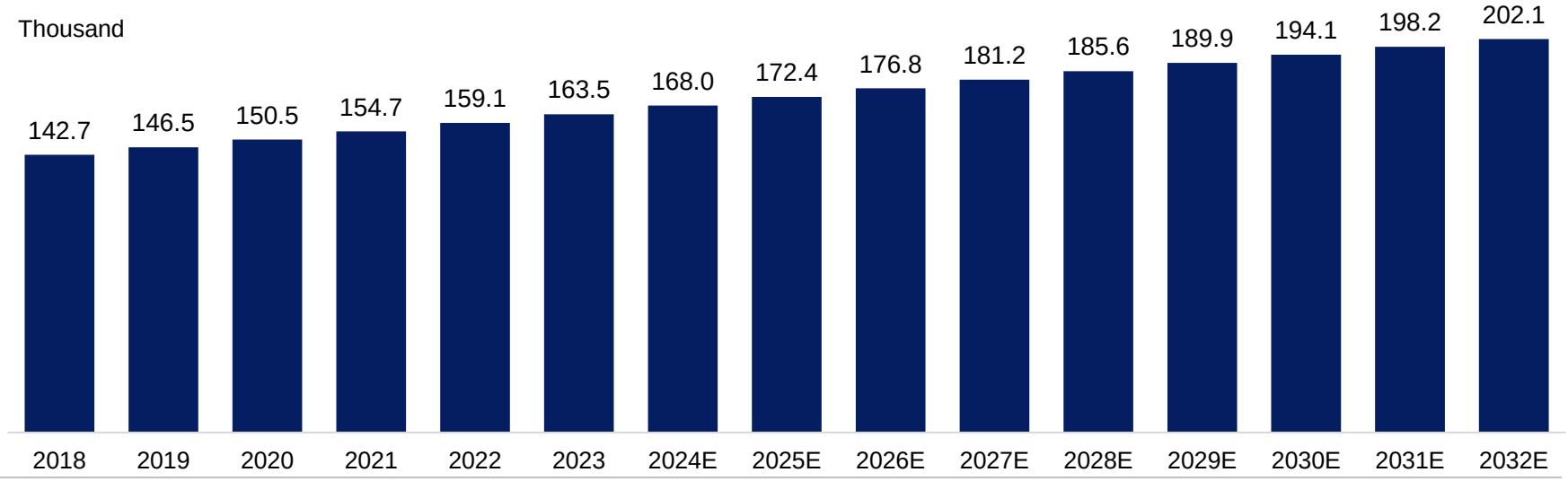
Source: Frost & Sullivan analysis

Incidence of SCLC in China, 2018-2032E

- Between 2018 and 2023, the number of SCLC cases in China grew from 142.7 thousand to 163.5 thousand, reflecting a CAGR of 2.8%. Projections suggest that by 2028, the incidence will increase to 185.6 thousand cases, with a CAGR of 2.6%. By 2032, the incidence is anticipated to rise to 202.1 thousand cases, growing at a CAGR of 2.2%.

Incidence of SCLC in China 2018-2032E

	CAGR
2018-2023	2.8%
2023-2028E	2.6%
2028E-2032E	2.2%



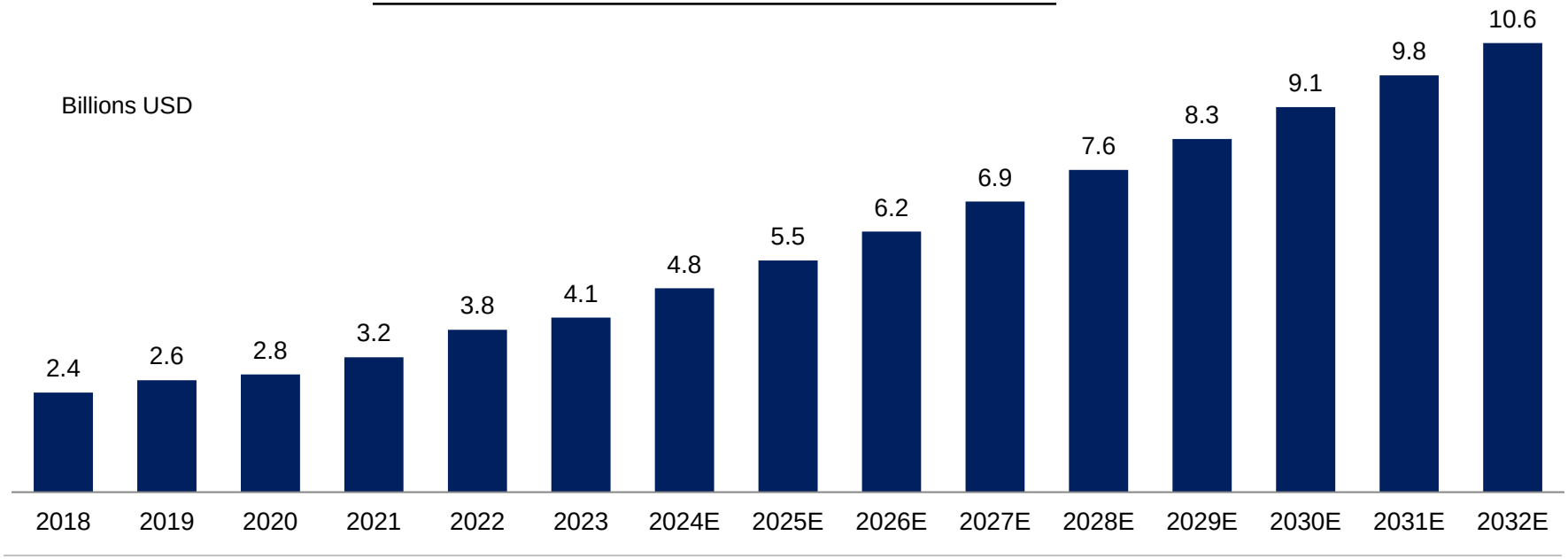
Source: Frost & Sullivan analysis

Global SCLC Drug Market Size, 2018-2032E

- Global SCLC drug market is estimated to increase from USD 4.1 billion in 2023 to 7.6 billion in 2028, with a CAGR of 13.0%. In the future, the global SCLC drug market will further increase to USD 10.6 billion in 2032, with a CAGR of 8.7% from 2028 to 2032.

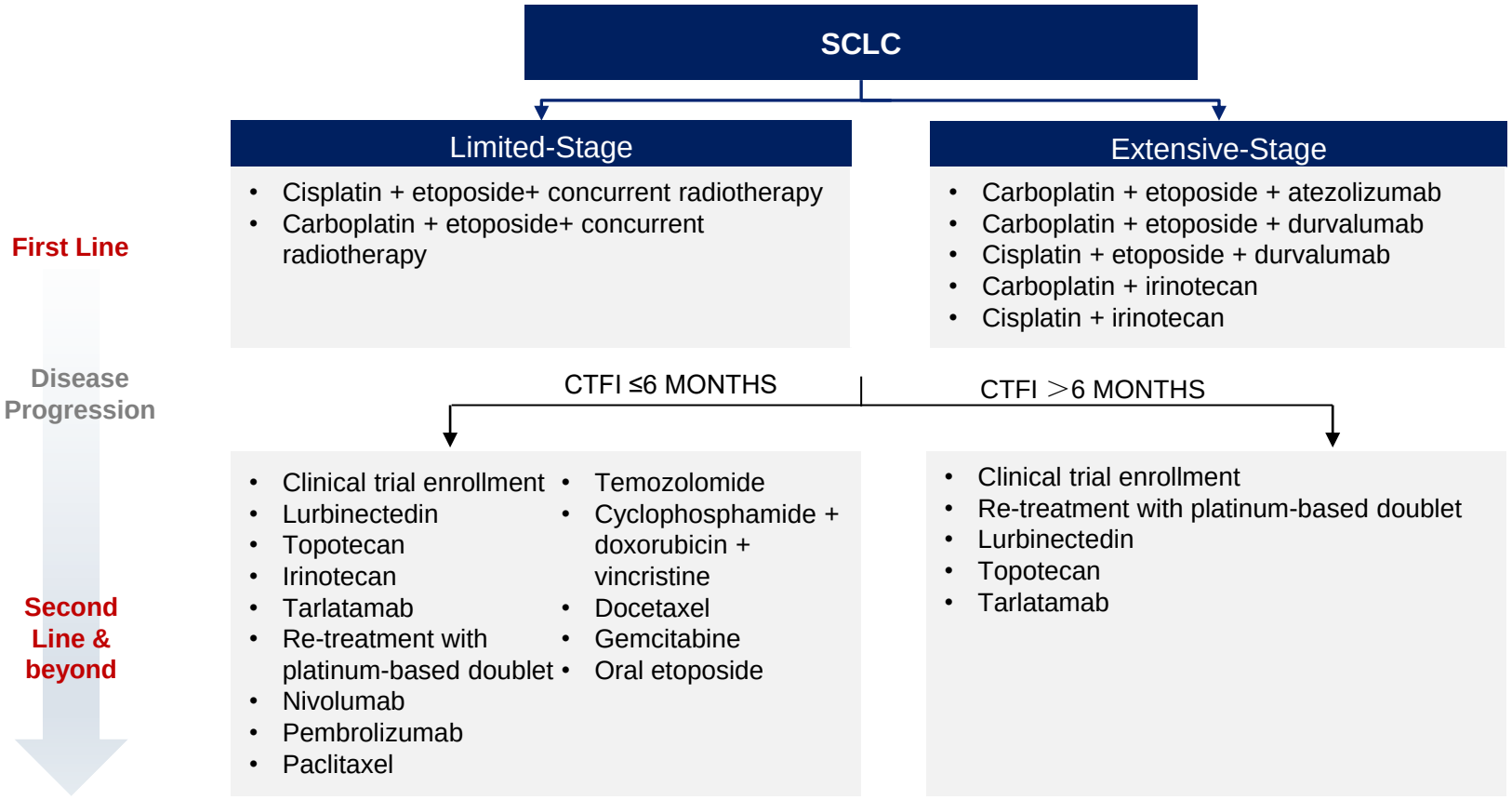
Global SCLC Drug Market Size, 2018-2032E

Period	CAGR
2018-2023	11.9%
2023-2028E	13.0%
2028E-2032E	8.7%



Source: Frost & Sullivan analysis

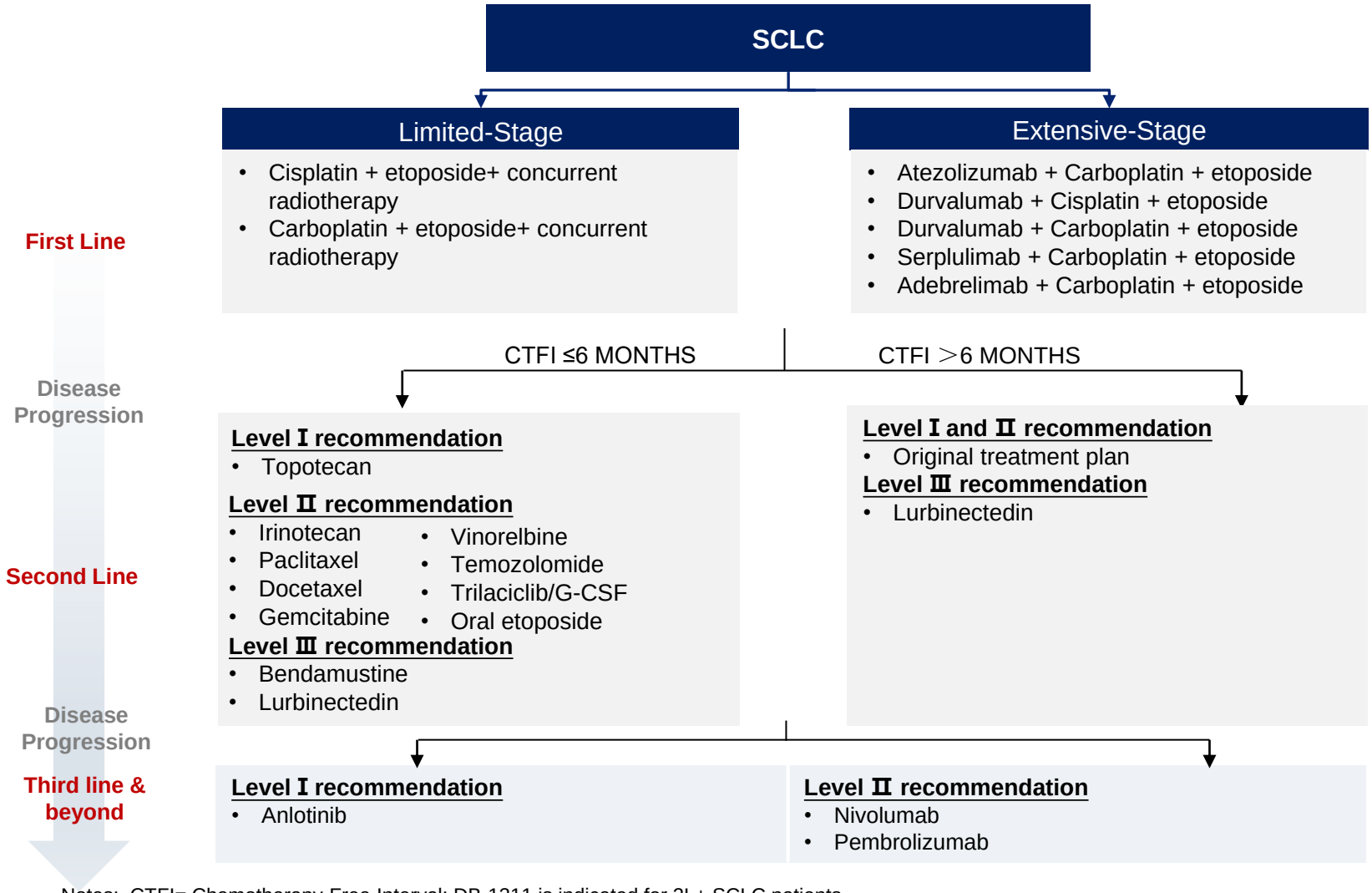
Treatment Paradigm of SCLC in U.S.



Notes:. CTFI= Chemotherapy-Free Interval; DB-1311 is indicated for 2L+ SCLC patients.

Source: NCCN 2024 , Frost & Sullivan Analysis

Treatment Paradigm of SCLC in China



Notes:. CTFI= Chemotherapy-Free Interval; DB-1311 is indicated for 2L+ SCLC patients.

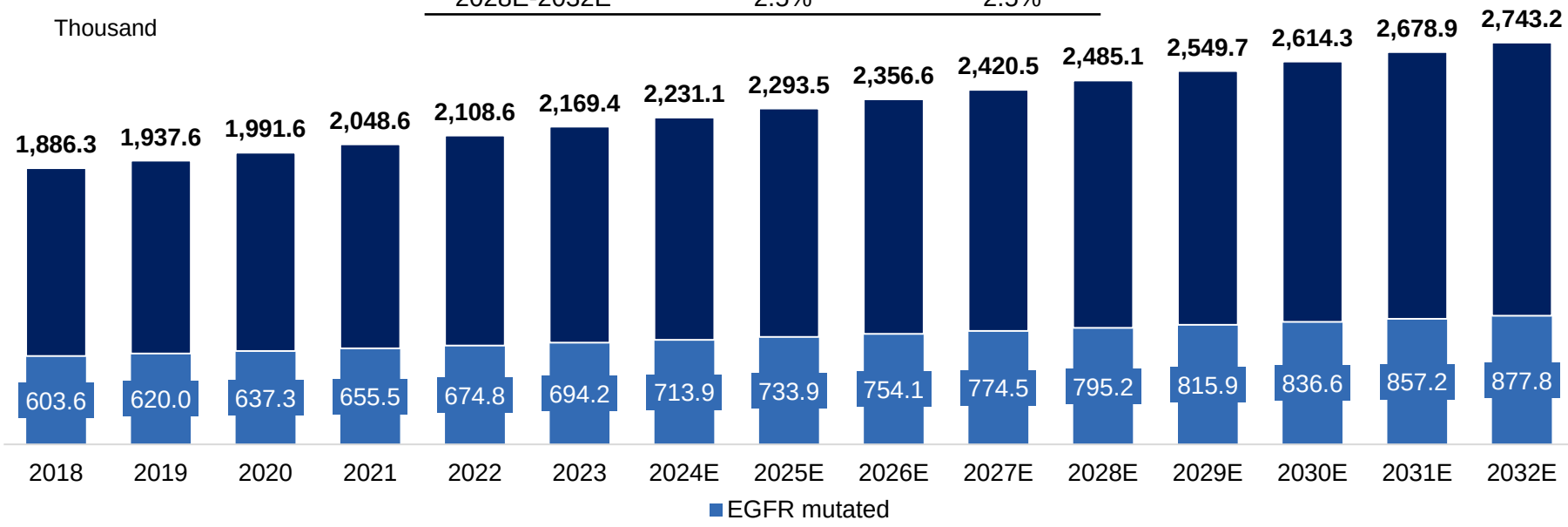
Source: CSCO 2024 , Frost & Sullivan Analysis

Incidence of NSCLC in Global, 2018-2032E

- Global incidence of NSCLC cases increased from 1,886.3 thousand in 2018 to 2,169.4 thousand in 2023, with a CAGR of 2.8%. The number is predicted to reach 2,485.1 thousand by 2028 and 2,743.2 thousand by 2032. The CAGR between 2028-2032 is 2.5%.
- By 2023, the number of cases worldwide with EGFR mutations would rise to 694.2 thousand, accounting for more than 30% of the whole cases.

Incidence of NSCLC in Global 2018-2032E

	CAGR	
	EGFR-mutated	Total
2018-2023	2.8%	2.8%
2023-2028E	2.8%	2.8%
2028E-2032E	2.5%	2.5%



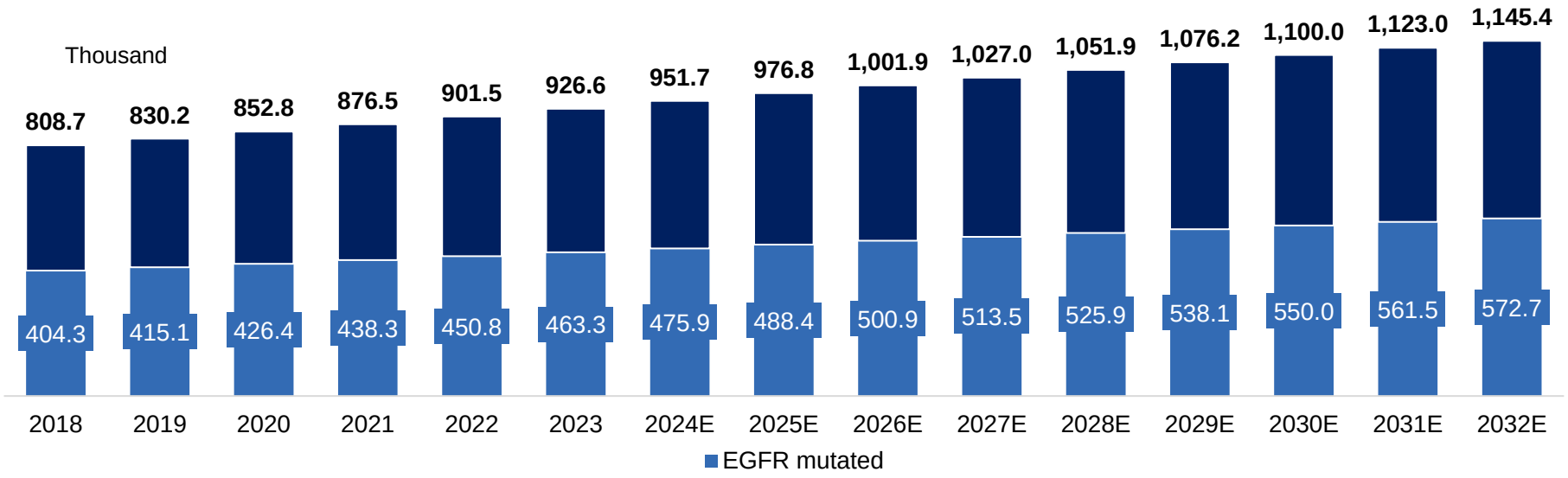
Source: Frost & Sullivan analysis

Incidence of NSCLC in China, 2018-2032E

- NSCLC cases increased from 808.7 thousand in 2018 to 926.6 thousand in 2023 , with a CAGR of 2.8%. By 2028 and 2032, the number of cases is predicted to reach 1,051.9 thousand and 1,145.4 thousand respectively.
- It is anticipated that the number of cases of EGFR-mutated NSCLC in China would rise from 404.3 thousand in 2018 to 572.7 thousand cases by 2032, accounting for around 50% of all NSCLC cases.

Incidence of NSCLC in China 2018-2032E

	CAGR	
	EGFR-mutated	Total
2018-2023	2.8%	2.8%
2023-2028E	2.6%	2.6%
2028E-2032E	2.2%	2.2%



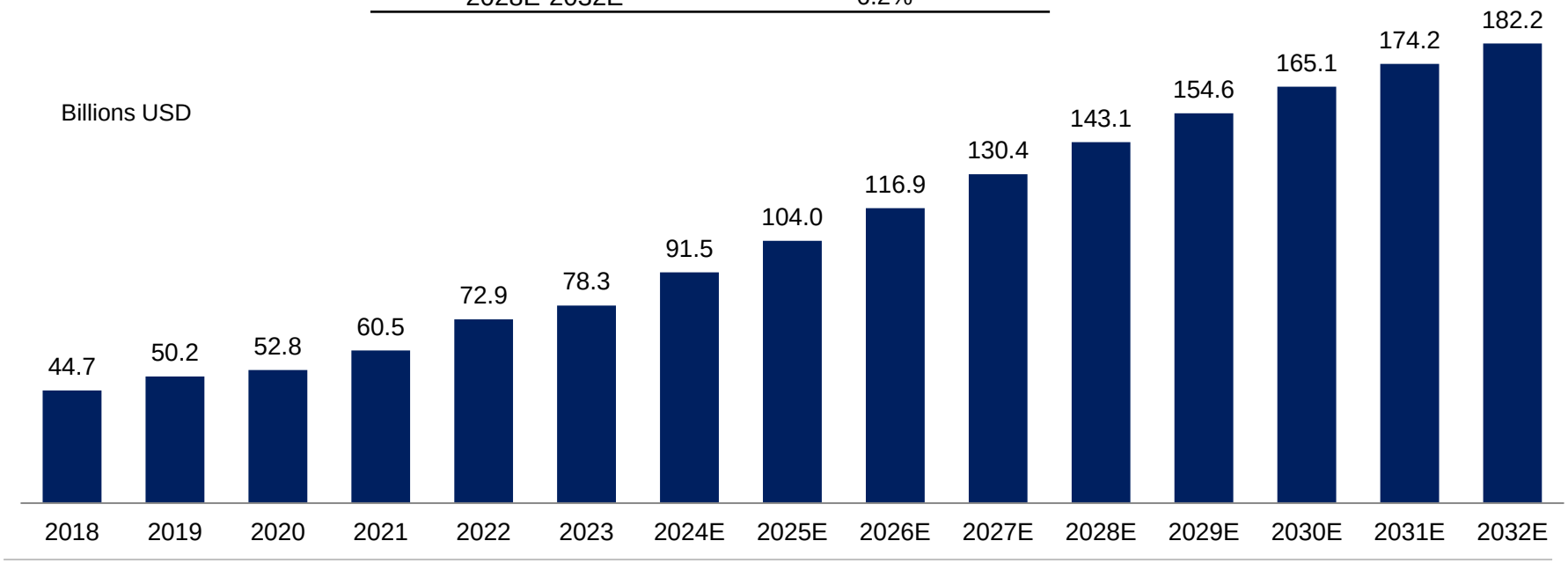
Source: Frost & Sullivan analysis

Global NSCLC Drug Market Size, 2018-2032E

- Global NSCLC drug market is estimated to increase from USD 78.3 billion in 2023 to 143.1 billion in 2028, with a CAGR of 12.8%. In the future, the global NSCLC drug market will further increase to USD 182.2 billion in 2032, with a CAGR of 6.2% from 2028 to 2032.

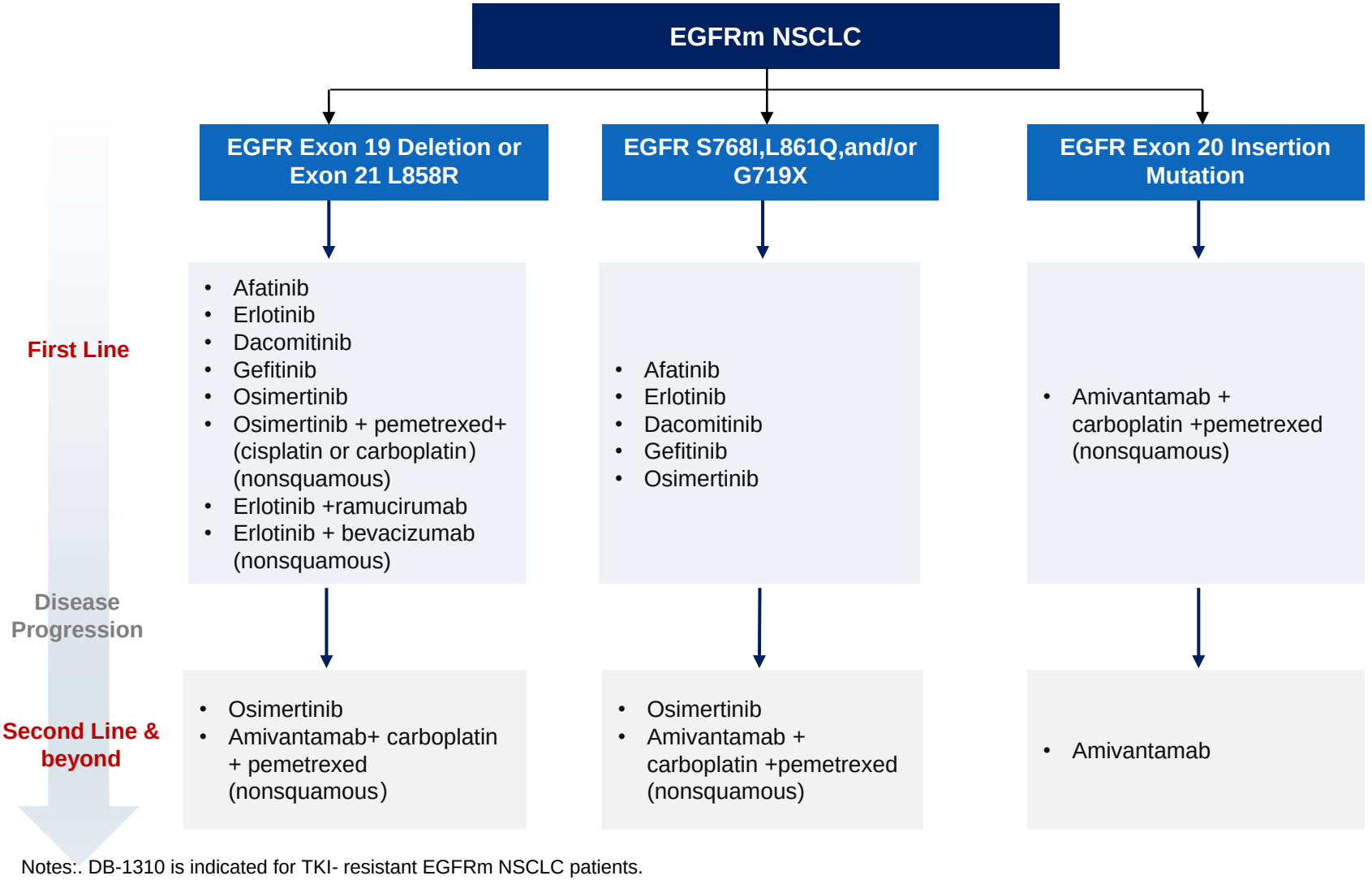
Global NSCLC Drug Market Size, 2018-2032E

Period	CAGR
2018-2023	11.9%
2023-2028E	12.8%
2028E-2032E	6.2%



Source: Frost & Sullivan analysis

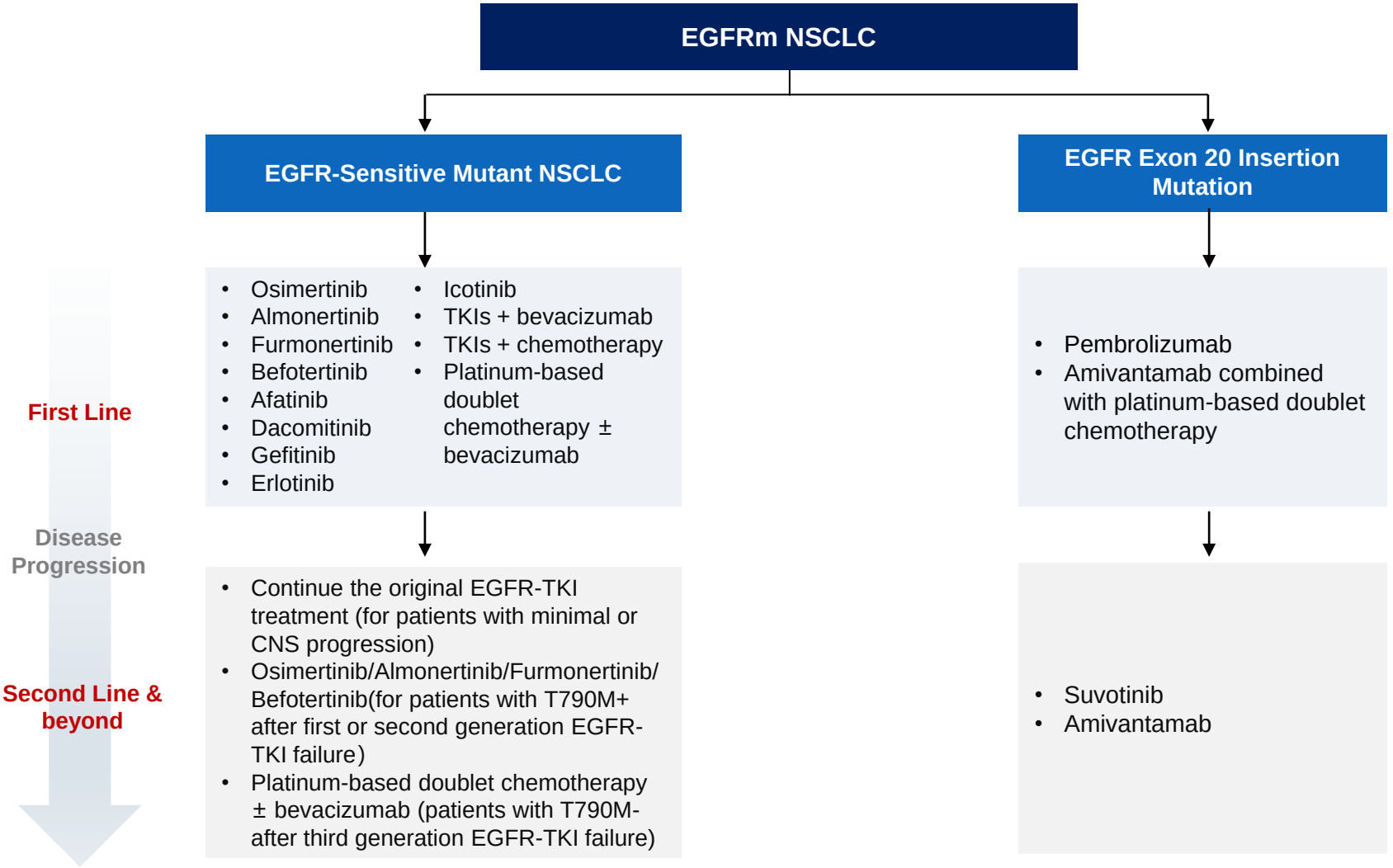
Treatment Paradigm of EGFRm NSCLC in U.S.



Notes:. DB-1310 is indicated for TKI- resistant EGFRm NSCLC patients.

Source: NCCN 2024, Frost & Sullivan Analysis

Treatment Paradigm of EGFRm NSCLC in China



Notes:. DB-1310 is indicated for TKI- resistant EGFRm NSCLC patients.

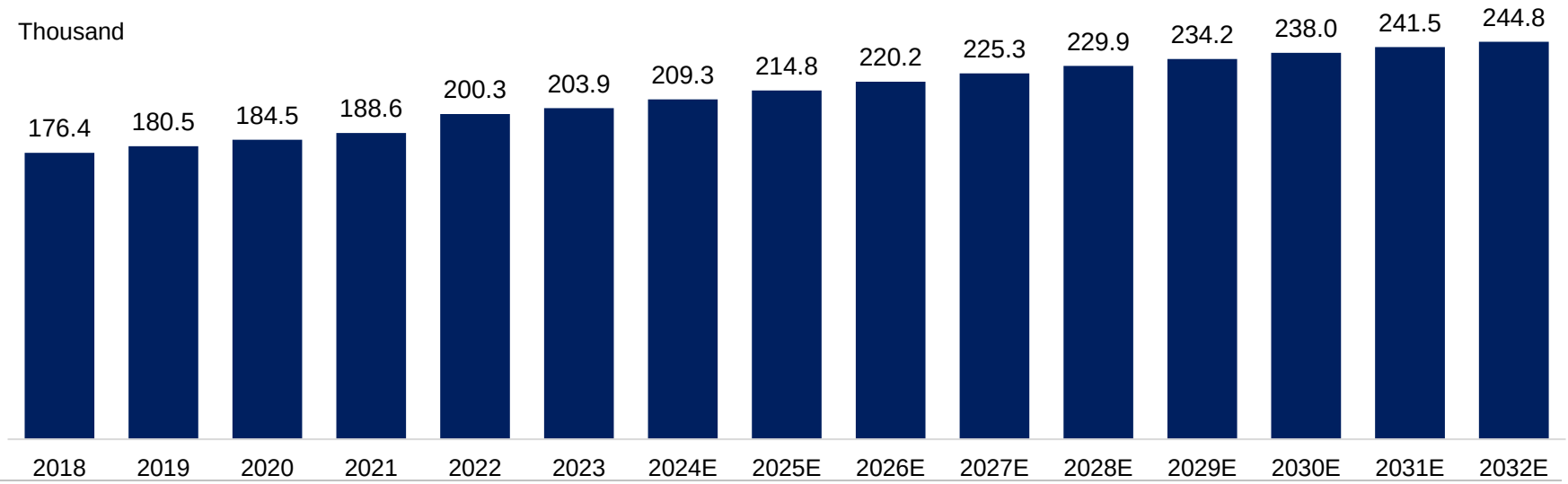
Source: CSCO 2024, Frost & Sullivan Analysis

Incidence of mCRPC in Global, 2018-2032E

- The incidence of mCRPC globally increased from 176.4 thousand cases in 2018 to 203.9 thousand cases in 2023, with a CAGR of 2.9%. According to projections, the incidence will increase to 229.9 thousand cases by 2028, representing a 2.4% CAGR. By 2032, it is expected to reach 244.8 thousand cases, with a CAGR of 1.6%.

Incidence of mCRPC in Global, 2018-2032E

	CAGR
2018-2023	2.9%
2023-2028E	2.4%
2028E-2032E	1.6%



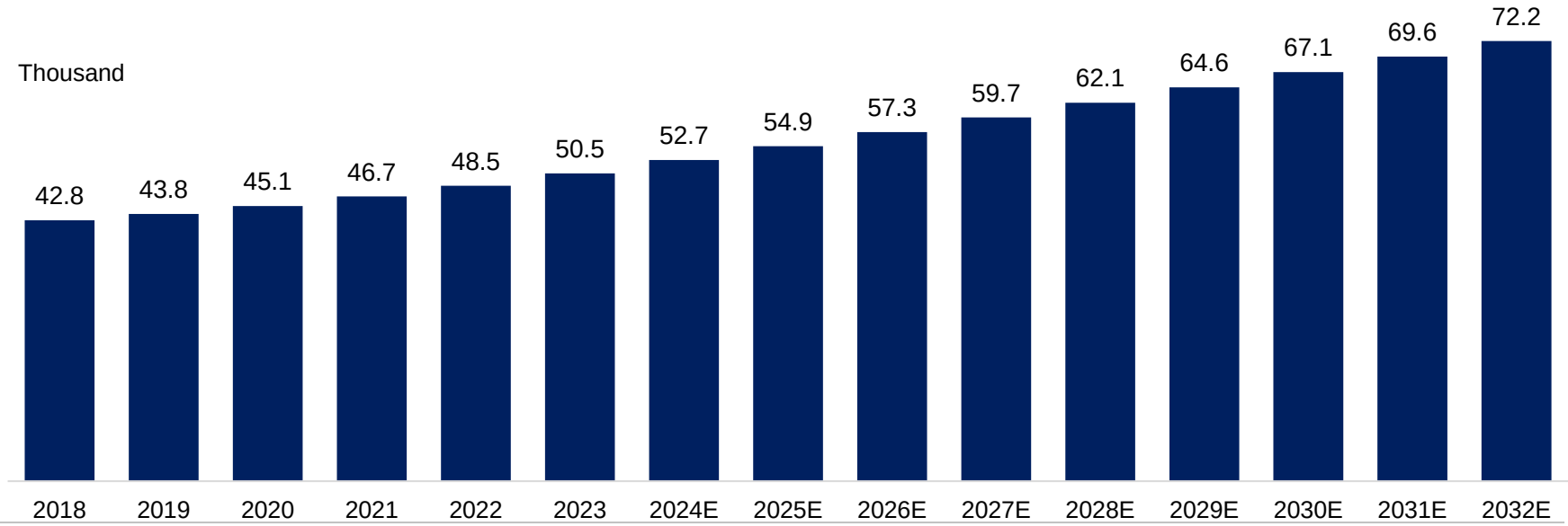
Source: Frost & Sullivan analysis

Incidence of mCRPC in China, 2018-2032E

- The incidence of mCRPC in China increased from 42.8 thousand cases in 2018 to 50.5 thousand cases in 2023, with a CAGR of 3.4%. Projections indicate that the incidence will reach 62.1 thousand cases by 2028, with a CAGR of 4.2% between 2023-2028 and 72.2 thousand cases by 2032, with a CAGR of 3.8% between 2028-2032.

Incidence of mCRPC in China, 2018-2032E

	CAGR
2018-2023	3.4%
2023-2028E	4.2%
2028E-2032E	3.8%



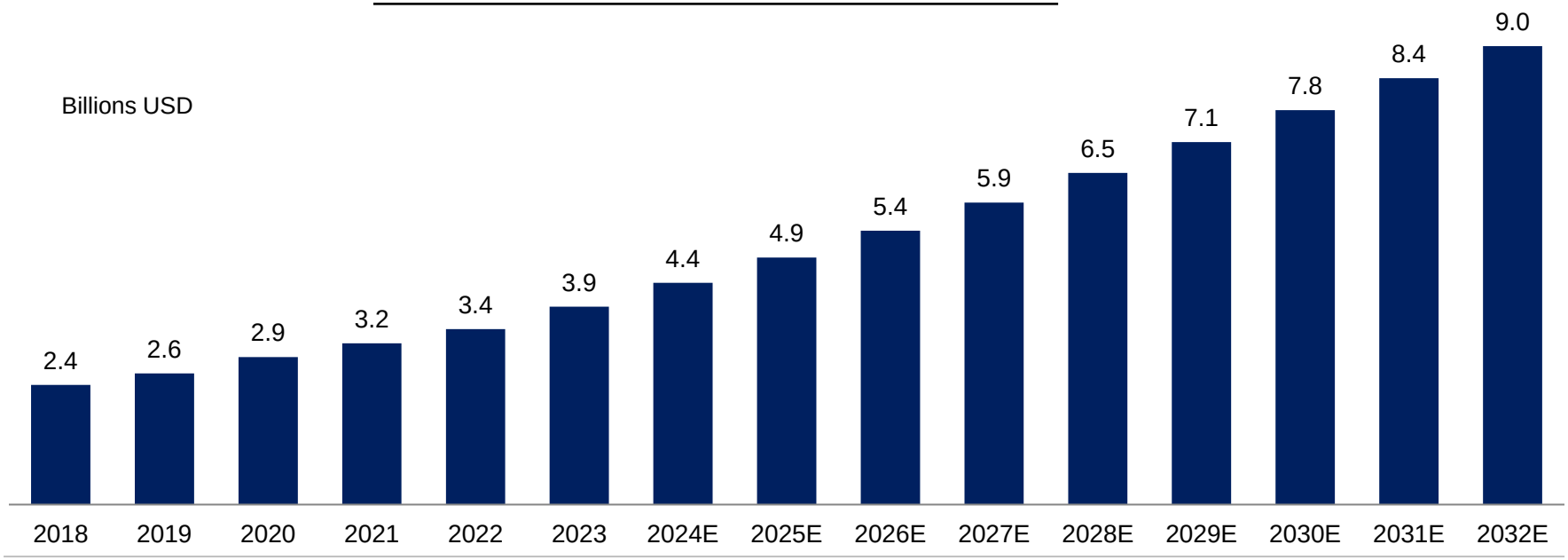
Source: Frost & Sullivan analysis

Global CRPC Drug Market Size, 2018-2032E

- The global CRPC drug market size reached USD 3.9 billion in 2023, with a CAGR of 10.6% from 2018 to 2023. The market size is expected to reach USD 6.5 billion in 2028, with a CAGR of 10.9% from 2023 to 2028. The market will further grow to USD 9.0 billion in 2032, with a CAGR of 8.4% from 2028 to 2032.

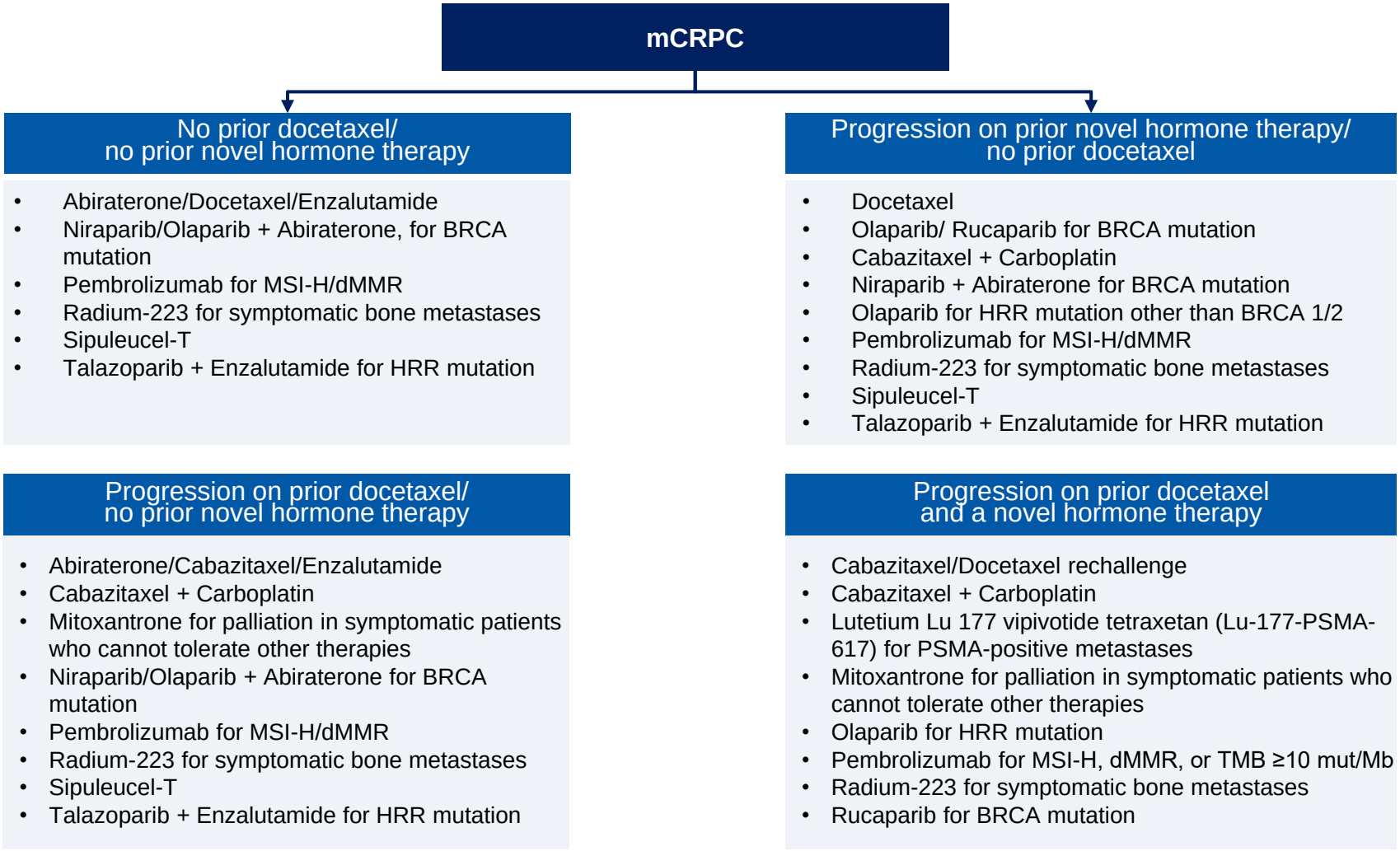
Global CRPC Drug Market Size, 2018-2032E

Period	CAGR
2018-2023	10.6%
2023-2028E	10.9%
2028E-2032E	8.4%



Source: Frost & Sullivan analysis

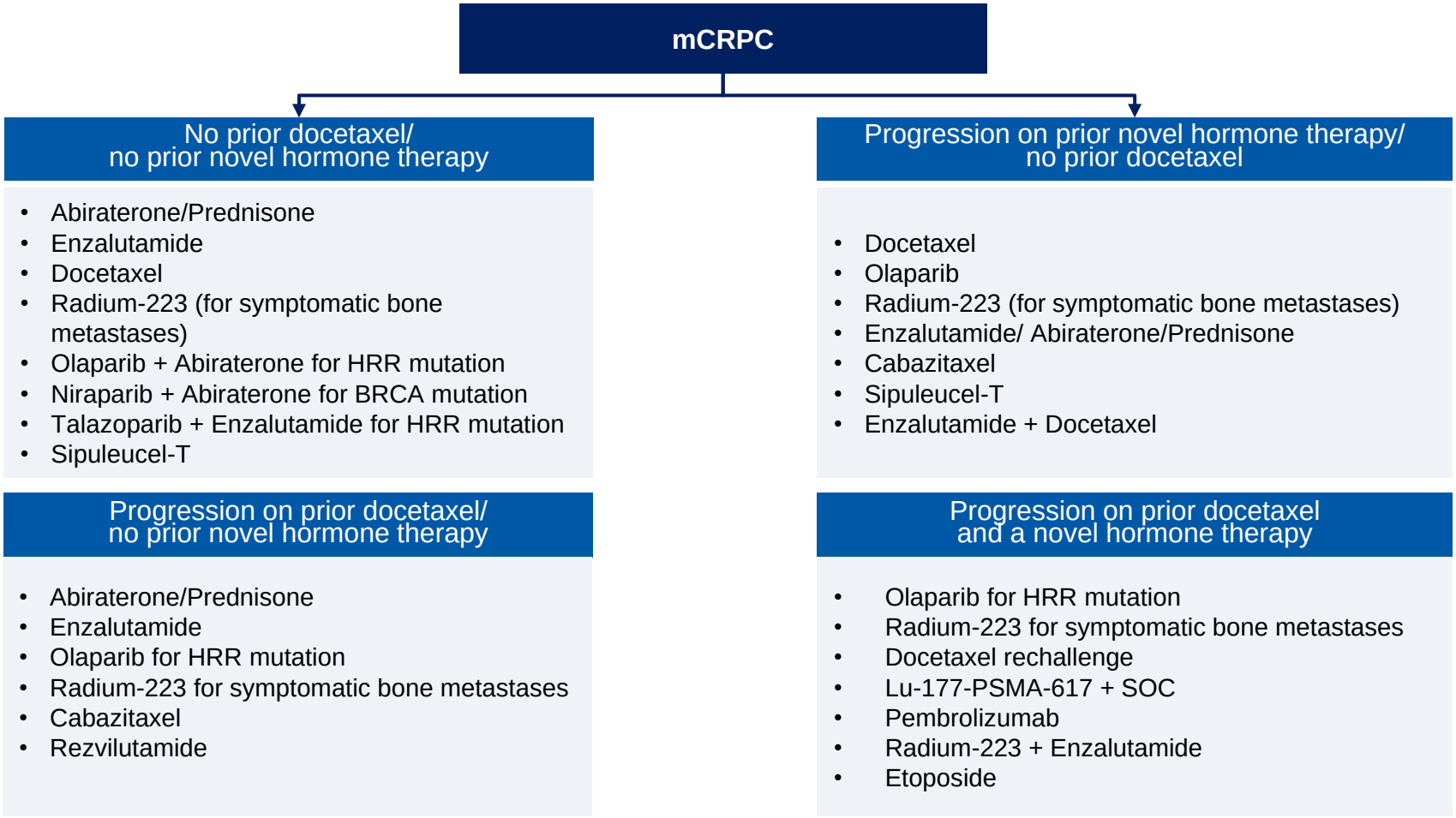
Treatment Paradigm of mCRPC in U.S.



Notes:. DB-1311 is indicated for late line CRPC patients.

Source: NCCN 2024, Frost & Sullivan Analysis

Treatment Paradigm of mCRPC in China



Notes:. DB-1311 is indicated for late line CRPC patients.

Source: CSCO 2024, Frost & Sullivan Analysis

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Competitive Landscape of MRCT HER-3 ADC Trials

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
U3-1402	EGFRm NSCLC	NDA	Daiichi Sankyo/Merck Sharp & Dohme	2023-12-22	Global
	Solid Tumors	Phase 2		2023-12-15	Global
	Gastrointestinal Cancers	Phase 1/2		2024-09-19	Global
	NSCLC	Phase 1		2017-08-24	Global
DB-1310	Solid Tumors	Phase 1/2a	DualityBio	2023-03-27	Global
SHR-A2009	Solid tumors	Phase 1	Hengrui Pharmaceuticals	2021-11-10	Global
YL202/BNT 326	NSCLC and BC	Phase 1	MediLink/BioNtech	2022-12-16	U.S., China

By March 28th. 2025

Note: Global means ≥ 3 countries

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Competitive Landscape of non-MRCT HER-3 ADC Trials

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
SHR-A2009	EGFRm NSCLC	Phase 3	Hengrui Pharmaceuticals	2024-11-04	China
	Solid Tumors	Phase 1b/2		2023-10-08	China
	BC	Phase 1/2		2024-01-25	China
U3-1402	BC	Phase 2	Daiichi Sankyo/Merck Sharp & Dohme	2021-01-07	U.S.
	BC and NSCLC brain metastases	Phase 2		2023-05-19	Austria, Spain
	HER3+ BC	Phase 1/2		2016-12-02	U.S., Japan
YL202/BNT326	Solid Tumors	Phase 2	MediLink/BioNtech	2023-10-30	China
	mTNBC	Phase 2		2024-06-03	China
IBI133	Solid Tumors	Phase 1/2	Innovent	2023-12-14	Australia
AMT-562	Solid Tumors	Phase 1	Multitude Therapeutics	2024-01-10	Australia
SIBP-A13	Solid Tumors	Phase 1	Shanghai Institute Of Biological Products	2024-02-19	China
AK138D1	Solid Tumors	Phase 1	Akeso	2024-12-12	Australia

By March 28th. 2025

Note: Global means ≥ 3 countries

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

TROP-2 Expressions and Potential Indications

- TROP-2 is a transmembrane glycoprotein encoded by the tacstd2 gene. Over-expression of TROP2 was reported to predict poor prognosis in various solid tumors in number of studies. It is especially overexpressed in many types of cancers, such as gastric cancer, NSCLC, breast cancer etc. The table below includes common cancers that TROP2 usually expressed.

Cancer	TROP-2 Expression Ratio
Breast Cancer	80%
NSCLC	64-75%
Gastric Cancer	66%
Epithelial Ovarian Cancer	91%
Urothelial Carcinomas	90%
Pancreatic Cancer	87%
Cervical Cancer	89-98%
CRPC	89%
Endometrial Endometrioid Carcinoma	96%

Source: Literature Review, Frost & Sullivan Analysis

Global Marketed TROP-2 ADCs

Drugs	Company	Payload	Linker	Indication	Treatment Line	FDA Approval	NMPA Approval	Price	NRDL inclusion	U.S. Insurance/ Assistance Program coverage	Patent Expiry Date	S (r
Trodelvy (Sacituzumab govitecan;IMMU-132)	Gilead	SN-38	CL2A (Cleavable)	mTNBC	≥3L	2020.04	2022.06	US $2,604/180mg	No	100%	2028 (US) 2029 (EU)	1
				mUC	≥2L	2021.04	N/A					
				HR+/HER2- BC	≥3L	2023.02	2025.03					
佳泰莱 (Sacituzumab Tirumotecan; SKB264)	Kelun-Biotech/ Merck Sharp & Dohme	T030	CL2A (Cleavable)	mTNBC	≥3L	N/A	2024.11	RMB 9,399/200mg	No	N/A	2038 (China)	
				EGFRm NSCLC	≥3L		2025.03					
Datroway (datopotamab deruxtecan-dlnk)	Daiichi Sankyo /AstraZeneca	DXD	Glycine-glycine-phenylalanine-glycine (Cleavable)	HR+/HER2- BC	≥2L	2025.01	N/A	US $4,891/100mg	N/A	100%	2034 (US) 2034 (EU)	

By March 28th. 2025

Source: FDA, NMPA, Drug.com, Annual Report, Frost & Sullivan

Competitive Landscape of TROP-2 ADC in OC Globally

Drug Name	Indications	Highest Phase of Trial	Company	First Post Date	Location
SKB264/MK-2870	Platinum-sensitive OC	Phase 3	Kelun-Biotech/Merck Sharp & Dohme	2025-02-13	Global
	Solid Tumors, incl. OC	Phase 2		2022-12-08	Global
DS-1062a	Solid Tumors, incl. OC	Phase 2	Daiichi Sankyo /AstraZeneca	2022-08-05	Global
DB-1305/BNT325	Solid tumors, incl. OC, NSCLC and other cancers	Phase 1/2	DualityBio/BioNTech	2022-06-29	Global
SHR-A1921	OC	Phase 3	Hengrui Pharmaceuticals	2024-05-01	China
XYD-9668-198	Solid Tumors, incl. OC	Phase 1/2	Xinyunda Biotechnology	2023-04-21	China
BHV1510/GQ 1010	Solid Tumors, incl. OC	Phase 1/2	GeneQuantum/ Pyramid Biosciences	2024-05-09	China
FDA018	Solid Tumors, incl. OC	Phase 1	Fudan-Zhangjiang Bio-Pharmaceutical	2022-01-03	China
DXC1002	Solid Tumors, incl. OC	Phase 1	DAC Biotech	2023-12-26	China

By March 28th. 2025

Note: Global means ≥ 3 countries

Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Competitive Landscape of TROP-2 ADC combo with IO Trials

Drug Name	Indications	Combo IO Drug	Highest Phase of Trial	Company	First Post Date	Location
DS-1062a	NSCLC	PD-1 mAb	Phase 3	Daiichi Sankyo /AstraZeneca	2022-01-31	Global
	TNBC	PD-L1 mAb	Phase 3		2022-11-29	Global
	TNBC or HR-low/HER- BC	PD-L1 mAb+chemo	Phase 3		2023-11-01	Global
Sacituzumab Govitecan	TNBC	PD-1 mAb	Phase 3	Gilead Science	2022-05-19	Global
	NSCLC	PD-1 mAb+chemo	Phase 2		2022-01-11	Global
SKB264/MK-2870	HR+/HER2- BC	PD-1 mAb	Phase 3	Kelun-Biotech/ Merck Sharp & Dohme	2024-03-15	Global
	TNBC	PD-1 mAb	Phase 3		2024-05-01	Global
	Non sq-NSCLC	PD-1 mAb	Phase 3		2024-09-13	China
	NSCLC	PD-L1 mAb+chemo	Phase 2		2022-04-28	China
	HER2- BC	PD-L1 mAb	Phase 2		2022-07-06	China
	Solid tumors	PD-1 mAb	Phase 2		2022-12-08	Global
	UC	PD-1 mAb+chemo	Phase 1/2		2024-07-03	Global
DB-1305/BNT325	OC	PD-L1/VEGF-A bsAb	Phase 1/2	DualityBio/BioNTech	2022-06-29	Global
	NSCLC		Phase 1/2		2022-06-29	Global
	TNBC		Phase 1/2		2022-06-29	Global
	CC		Phase 1/2		2022-06-29	Global
SHR-1921	NSCLC	CTLA-4 mAb+PD-L1 mAb	Phase 1/2	Hengrui Pharmaceuticals	2024-05-30	China
BIO-106	Solid tumors	PD-1 mAb	Phase 1/2	BiOneCure Therapeutics	2022-04-11	U.S.
LCB84	Solid tumors	PD-1 mAb	Phase 1/2	LegoChem Biosciences	2023-07-12	U.S., Canada
BAT8008	Solid tumors	PD-1 mAb	Phase 1/2	Bio-Thera	2024-04-02	China

By March 28th. 2025

Note: only incl. trials ≥phase 1/2 ; Global means ≥ 3 countries

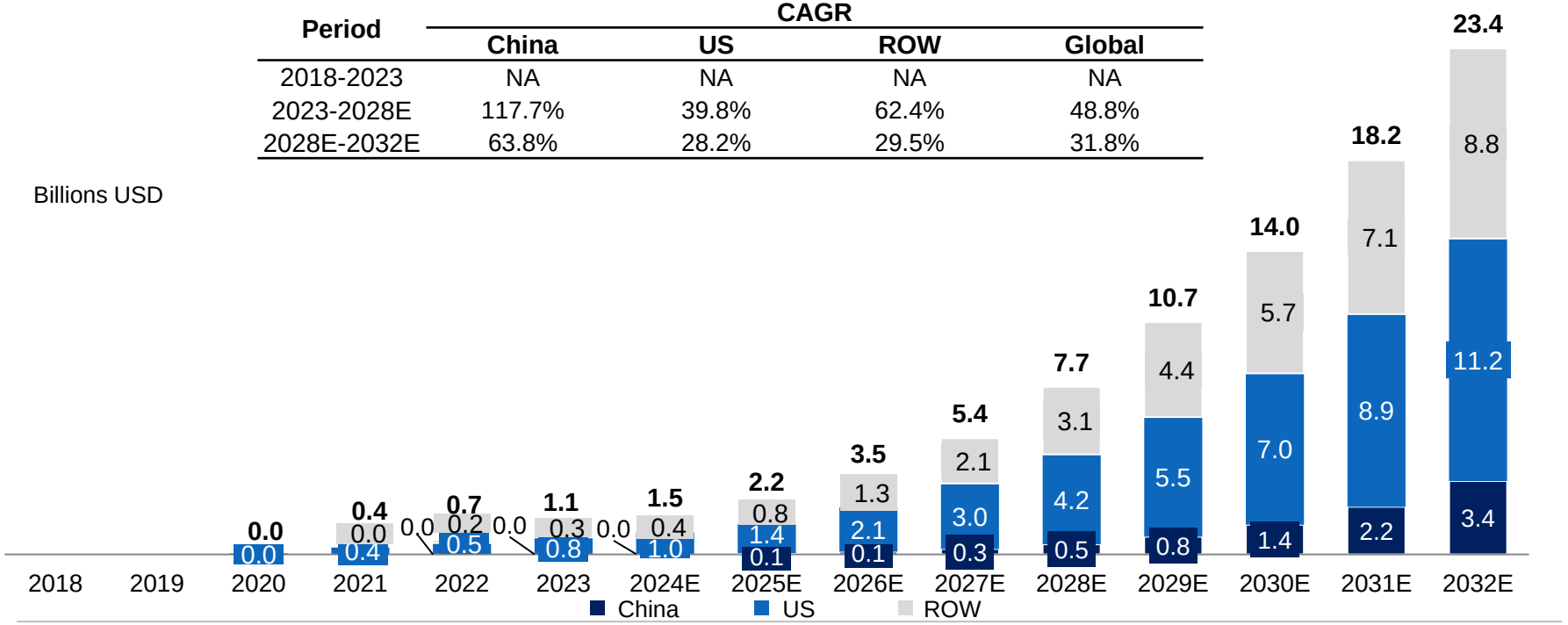
Source: ClinicalTrials, CDE, Frost & Sullivan Analysis

Global TROP2 ADCs Market Size, 2018-2032E

- The global TROP2 ADCs market is USD 1.1 billion in 2023. With the past success of indications expanding from breast cancer to uroepithelial carcinoma and the continued testing of new indications in the future, global TROP2 ADCs market will further increase to USD 7.7 billion in 2028 and USD 23.4 billion in 2032, with a CAGR of 48.8% between 2023-2028 and a CAGR of 31.8% between 2028-2032.
- The U.S TROP2 ADCs market is estimated to increase from USD 0.8 billion in 2023 to 4.2 billion in 2028, with a CAGR of 39.8%. It will further increase to USD 11.2 billion in 2032, with a CAGR of 28.2% from 2028 to 2032.
- In June 2022, the first targeted TROP2 ADC drug submitted by Everest Medicines was approved for marketing in China. Chinese TROP2 ADCs market is promising to reach USD 3.4 billion in 2032, with a CAGR of 117.7% between 2023-2028 and a CAGR of 63.8% between 2028-2032.

Global TROP2 ADCs Market Size, 2018-2032E

Period	CAGR			
	China	US	ROW	Global
2018-2023	NA	NA	NA	NA
2023-2028E	117.7%	39.8%	62.4%	48.8%
2028E-2032E	63.8%	28.2%	29.5%	31.8%



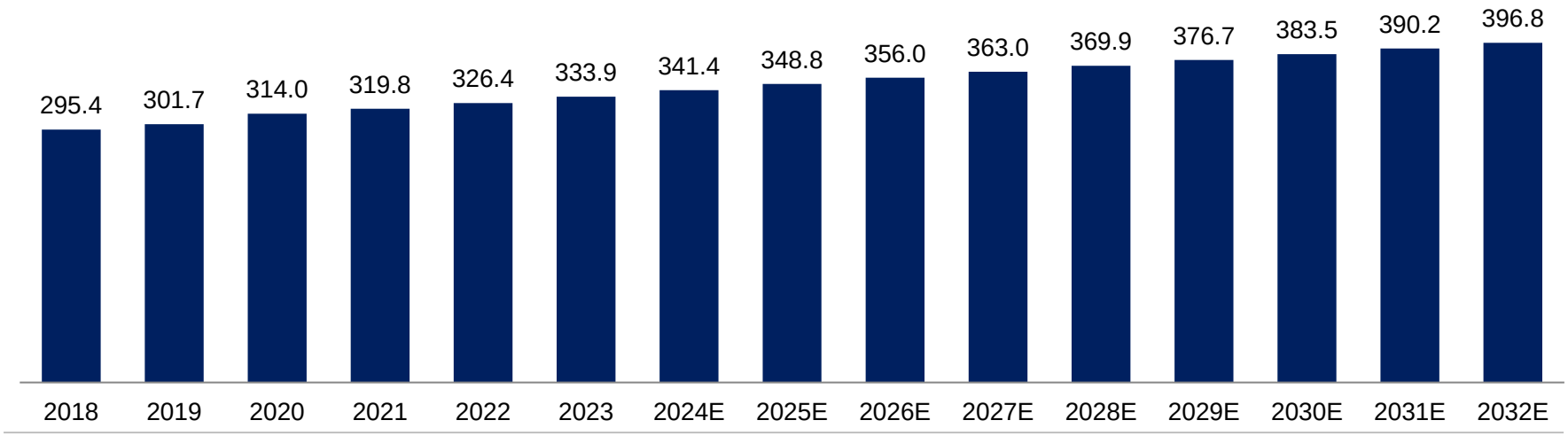
- Source: Frost & Sullivan analysis

Incidence of Ovarian Cancer in Global, 2018-2032E

- The global incidence of ovarian cancer rose from 295.4 thousand to 333.9 thousand between 2018 and 2023, showing a CAGR of 2.5%. Projections suggest that this figure will further increase to 369.9 thousand by 2028, reflecting a CAGR of 2.1% from 2023 to 2028. By 2032, it is anticipated to reach 396.8 thousand, growing at a CAGR of 1.8%.

Incidence of Ovarian Cancer in Global, 2018-2032E

	CAGR
2018-2023	2.5%
2023-2028E	2.1%
2028E-2032E	1.8%



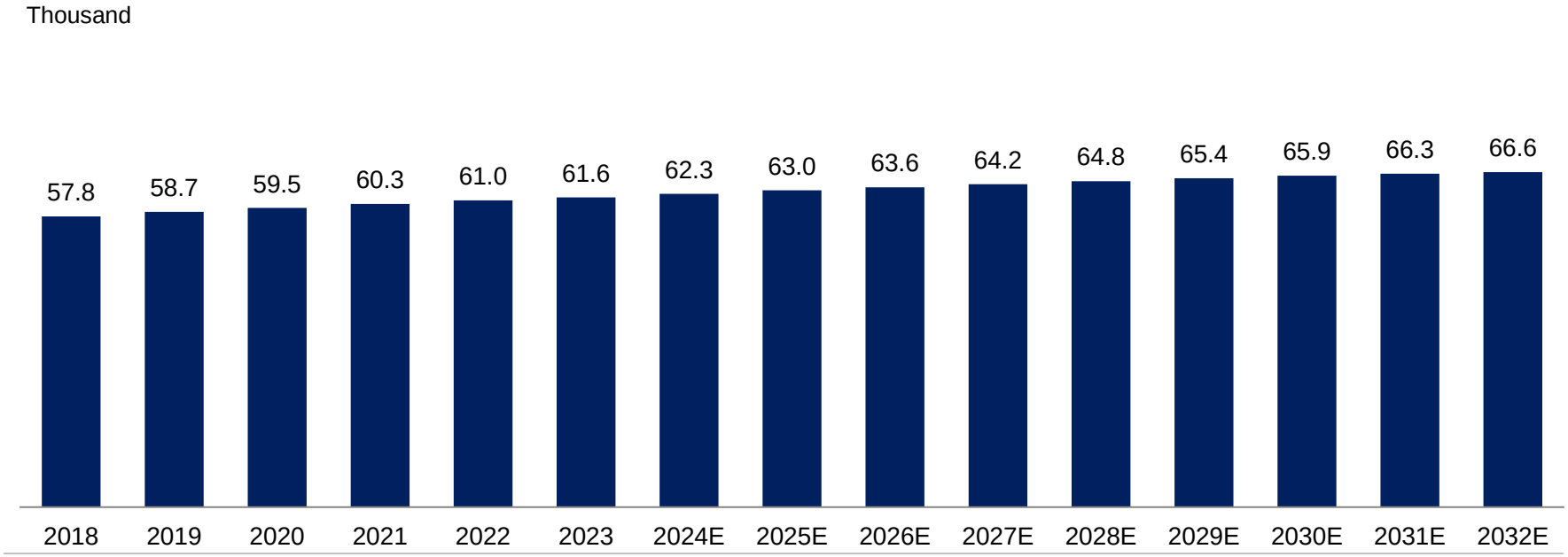
Source: Frost & Sullivan analysis

Incidence of Ovarian Cancer in China, 2018-2032E

- The incidence of ovarian cancer in China rose from 57.8 thousand to 61.6 thousand between 2018 and 2023, showing a CAGR of 1.3%. Projections suggest that this figure will further increase to 64.8 thousand by 2028, reflecting a CAGR of 1.0% from 2023 to 2028. By 2032, it is anticipated to reach 66.6 thousand, growing at a CAGR of 0.7%.

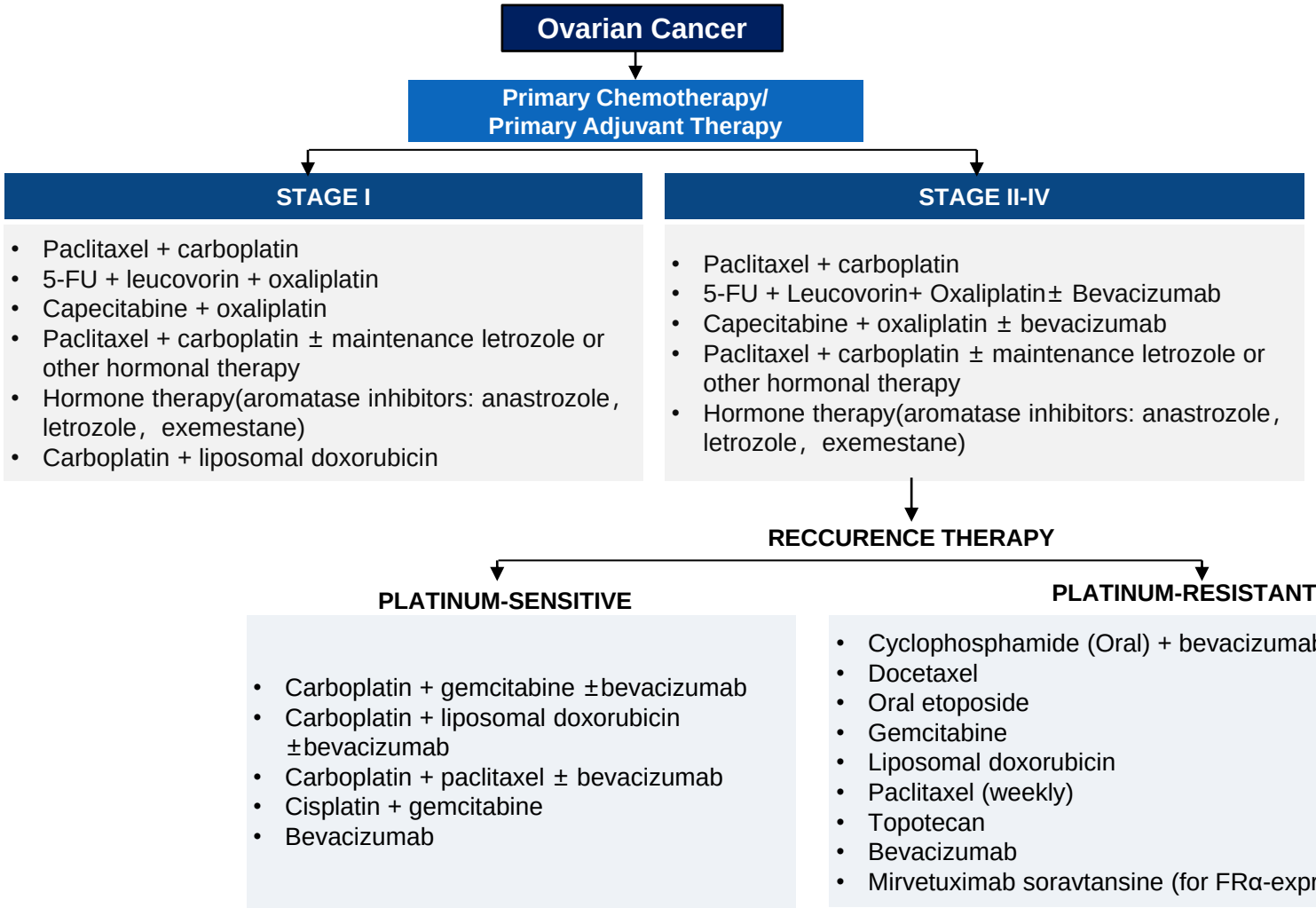
Incidence of Ovarian Cancer in China, 2018-2032E

	CAGR
2018-2023	1.3%
2023-2028E	1.0%
2028E-2032E	0.7%



Source: Frost & Sullivan analysis

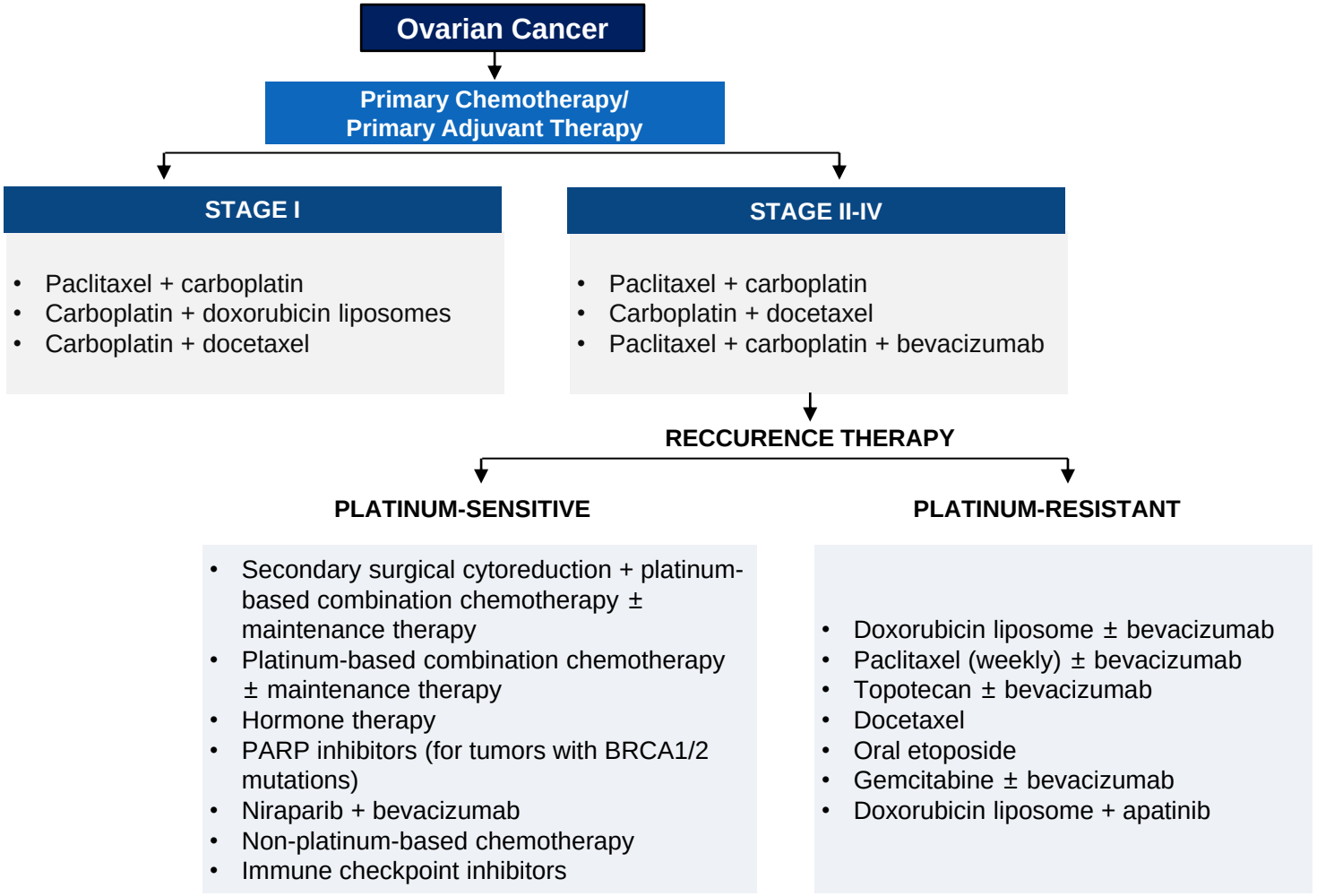
Treatment Paradigm of Ovarian Cancer in U.S.



Notes:. DB-1305 is indicated for 2L+ OC patients.

Source: NCCN 2024, Frost & Sullivan Analysis

Treatment Paradigm of Ovarian Cancer in China



Notes:. DB-1305 is indicated for 2L+ OC patients.

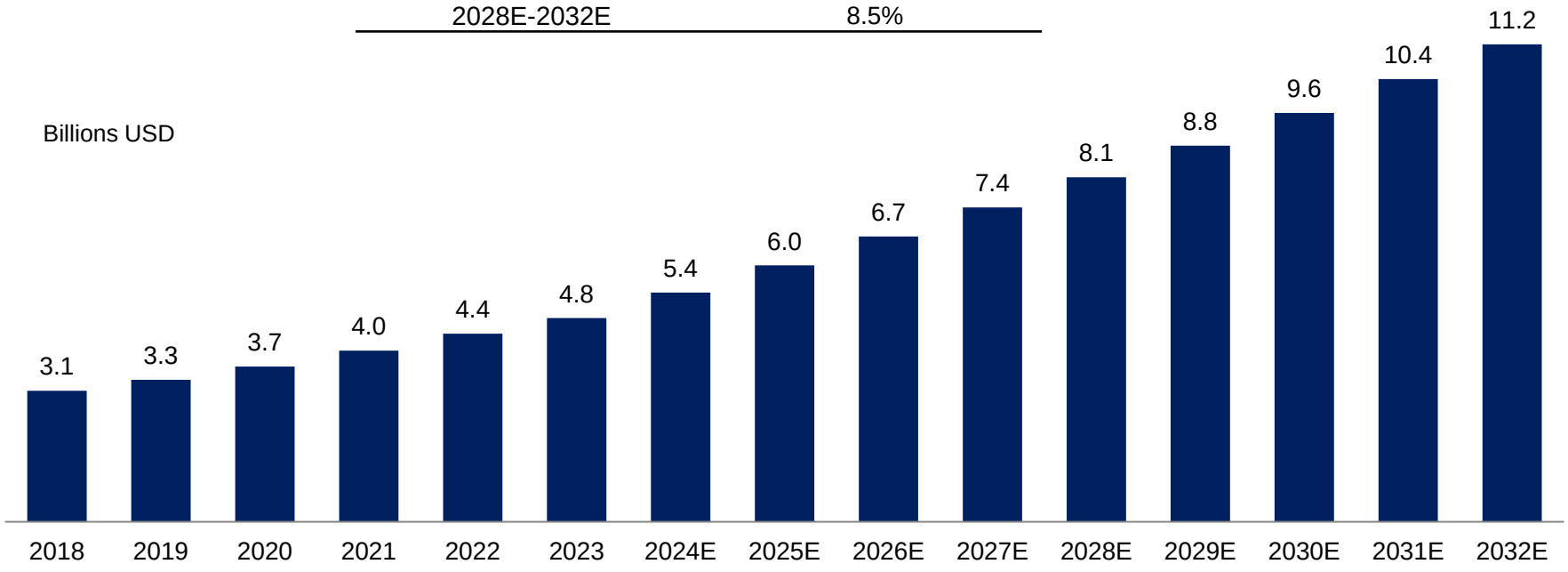
Source: CSCO 2024, Frost & Sullivan Analysis

Global Ovarian Cancer Drug Market Size, 2018-2032E

- The global ovarian cancer drug market size reached USD 4.8 billion in 2023, with a CAGR of 9.2% from 2018 to 2023. The market size is expected to reach USD 8.1 billion in 2028, with a CAGR of 11.1% from 2023 to 2028. The market will further grow to USD 11.2 billion in 2032, with a CAGR of 8.5% from 2028 to 2032.

Global Ovarian Cancer Drug Market Size, 2018-2032E

Period	CAGR
2018-2023	9.2%
2023-2028E	11.1%
2028E-2032E	8.5%



Source: Frost & Sullivan analysis

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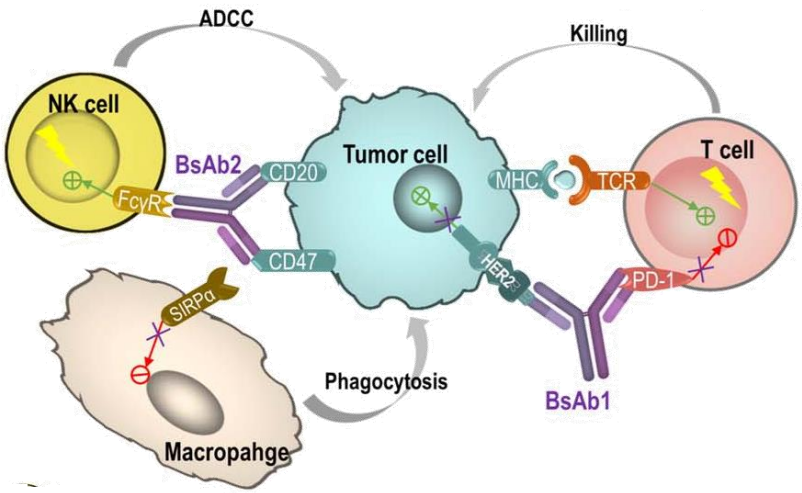
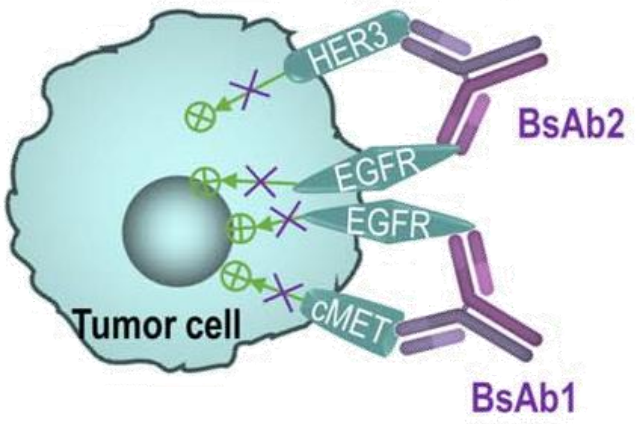
Mechanism of Action of BsADC

- Under TAA+IO approach, BsADCs are designed for binding to both one TAA to inhibit TAA signaling pathway and one immunomodulating receptor to regulate the immune system to attack the tumors.
- Dual TAAs targeting BsAb binds to double antigen-positive cancer cells, which offers several advantages including increased tumor selectivity, potential to concurrently modulate two functional pathways in the tumor cell and may yield improved payload delivery.

TAA+IO Approach



Dual-TAA Approach



Source: Development of bispecific antibodies in China: overview and prospects, Frost & Sullivan Analysis

B7-H3/PD-L1 Expressions and Potential Indications

- B7-H3 and PD-L1 are both immune checkpoint molecules. Their high expression on tumor cells can inhibit the activity of T cells, thus promoting tumor growth. Bispecific antibodies (bsAb) can enhance the anti-tumor activity of T cells and improve ADCC (antibody-dependent cell-mediated cytotoxicity) efficacy by simultaneously targeting B7-H3 and PD-L1, thereby selectively activating CD8+ T cells And enhance the natural killing power of tumors.
- High expression of PD-L1 is often associated with tumors evading immune surveillance, while high expression of B7-H3 is associated with tumor aggressiveness and poor prognosis. By jointly blocking these two immune checkpoints, bispecific antibodies can significantly improve anti-tumor efficacy. They can work together to treat cancers such as non-small cell lung cancer and small cell lung cancer.

Cancer	B7H3 Expression Ratio	PD-L1 Expression Ratio
Breast Cancer	57-74%	10-30%
Gastric Cancer	58%	40-65%
Hepatocellular Carcinoma	92%	17%
NSCLC	74%	24-60%
SCLC	65%	20-83%
CRPC	93%	50%

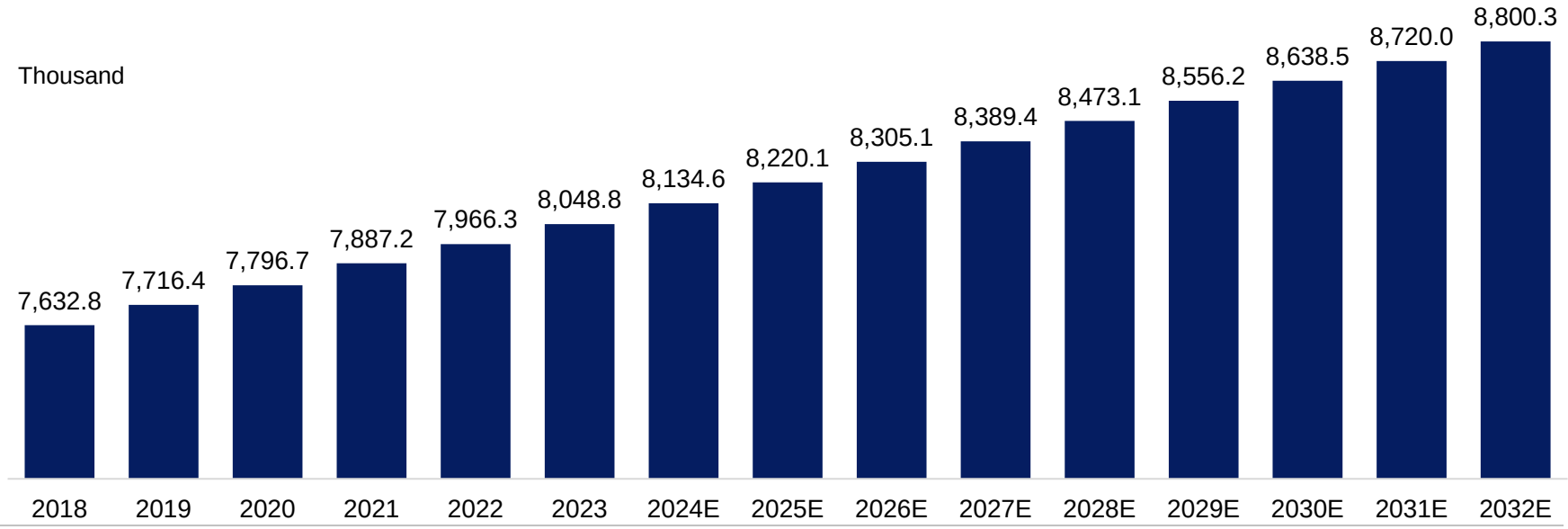
Source: Literature Review, Frost & Sullivan Analysis

Prevalence of SLE in Global, 2018-2032E

- The prevalence of SLE grew globally from 7,632.8 thousand cases in 2018 to 8,048.8 thousand cases in 2023 with a CAGR of 1.1%. It is predicted to increase at a CAGR of 1.0% to 8,473.1 thousand cases by 2028. The number of cases is then expected to increase further, with a 1.0% CAGR, to 8,800.3 thousand cases by 2032.

Prevalence of SLE in Global, 2018-2032E

	CAGR
2018-2023	1.1%
2023-2028E	1.0%
2028E-2032E	1.0%



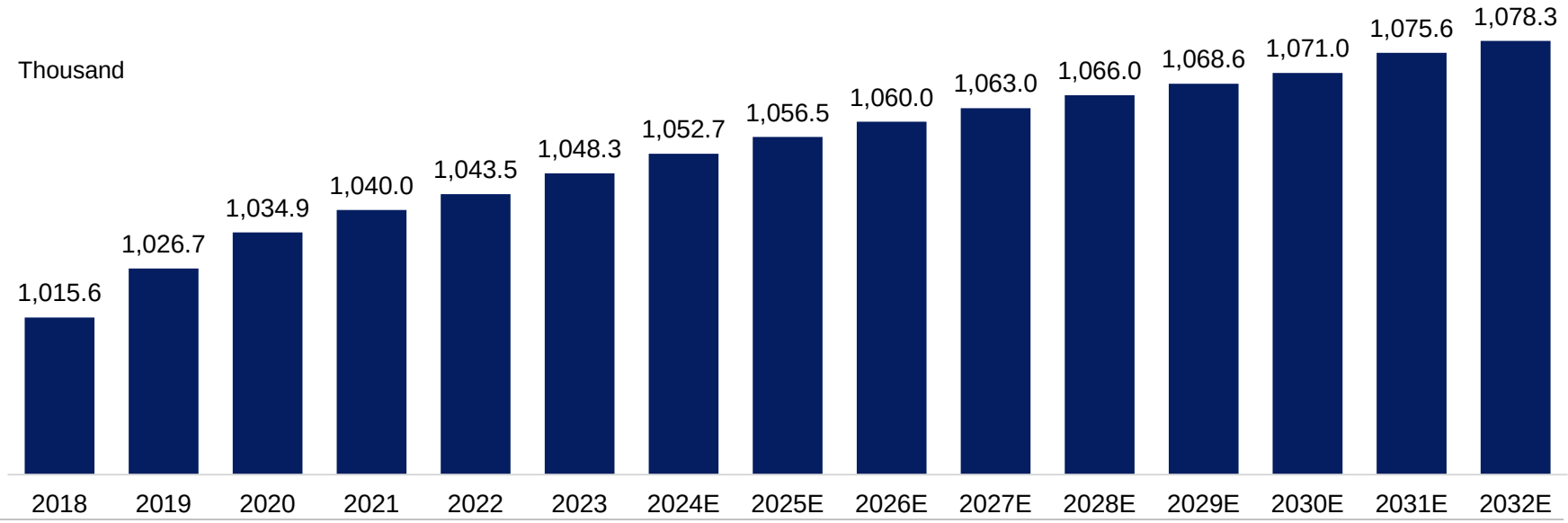
Source: Frost & Sullivan analysis

Prevalence of SLE in China, 2018-2032E

- In China, the prevalence of cases of SLE grew from 1,015.6 thousand in 2018 to 1,048.3 thousand in 2023, representing a 0.6% CAGR. With a CAGR of 0.3%, it is anticipated that there will be 1,066.0 thousand cases by 2028. With a 0.3% CAGR, it is predicted that the prevalence would reach 1,078.3 thousand cases by 2032.

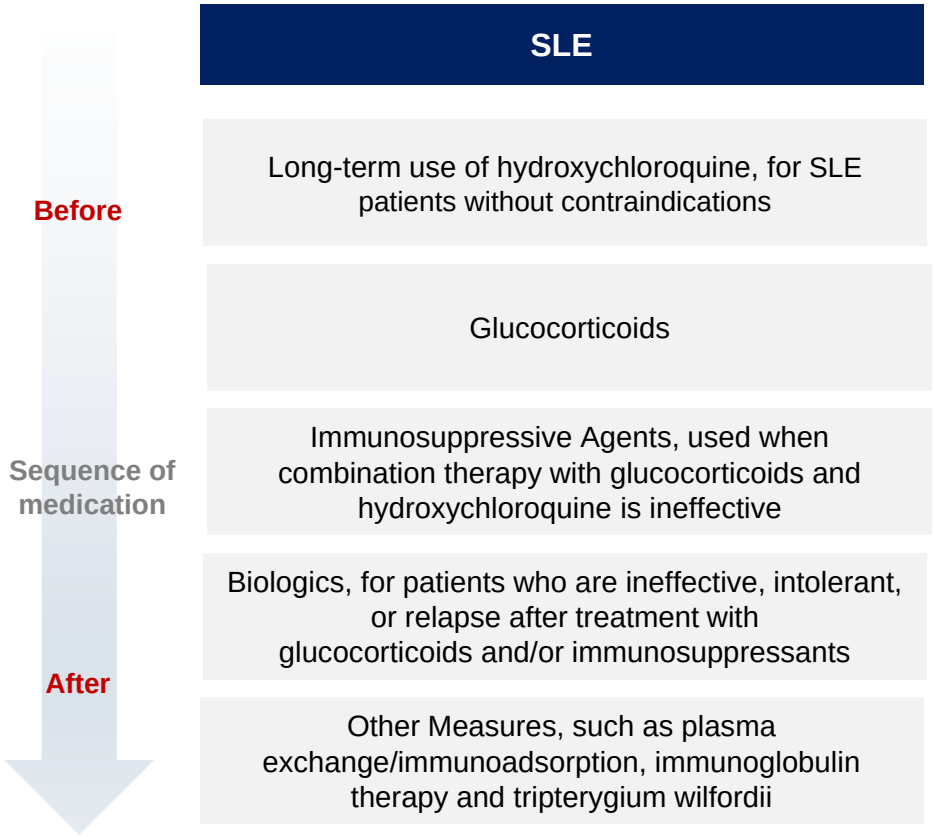
Prevalence of SLE in China, 2018-2032E

	CAGR
2018-2023	0.6%
2023-2028E	0.3%
2028E-2032E	0.3%



Source: Frost & Sullivan analysis

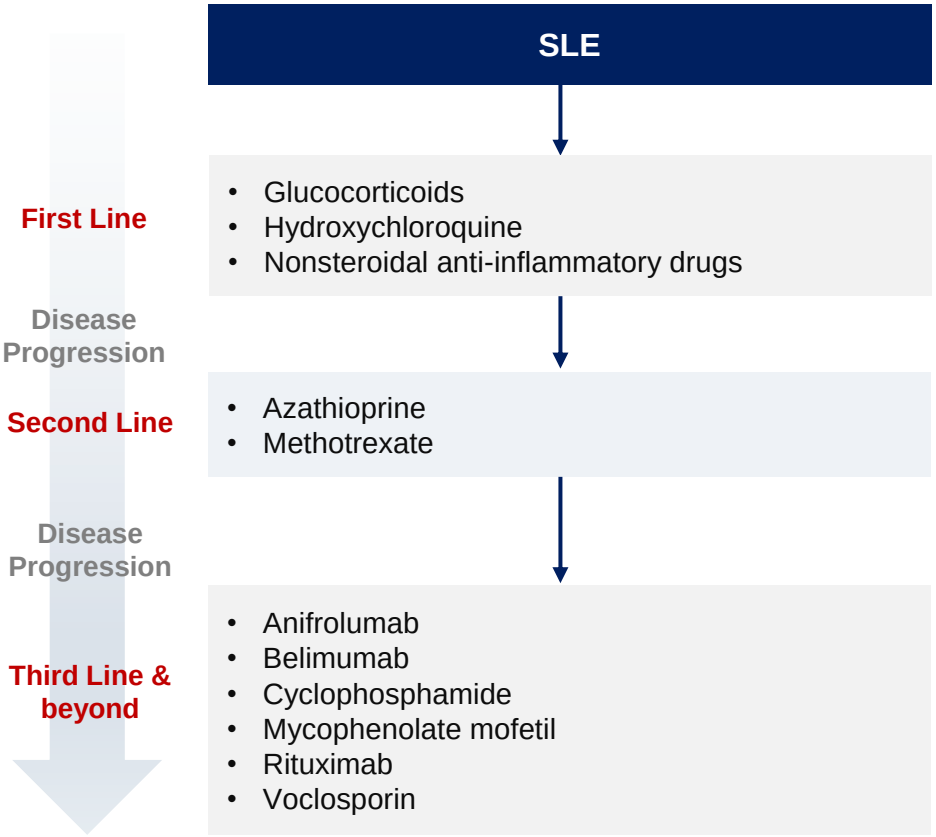
Treatment Paradigm of SLE in China



Notes:. DB-2304 is indicated for SLE patients.

Source: Guidelines for Diagnosis and Treatment of Systemic Lupus Erythematosus, Frost & Sullivan Analysis

Treatment Paradigm of SLE in U.S.

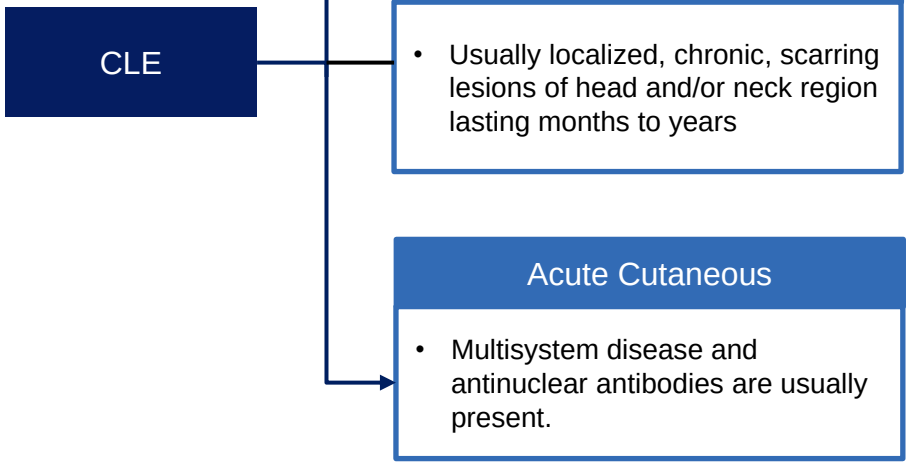


Notes:. DB-2304 is indicated for SLE patients.

Source: Systemic Lupus Erythematosus: Diagnosis and Treatment, Frost & Sullivan Analysis

Overview of CLE

- Cutaneous Lupus Erythematosus (CLE) is an autoimmune disease primarily affecting skin and mucosal tissue. It is typically classified into three main subtypes based on the disease chronicity, clinical morphology and distribution: acute (ACLE), subacute (SCLE), and chronic (CCLE)



Risk Factors

- Cigarette smoking
- Viral infections
- Trauma or injury to the skin
- Ultraviolet (UV) light exposure
- Genetics

Symptoms

- Clear discoid erythema and plaques
- Surface adhesion scales
- Shedding scales may indicate expansion of the hair follicle to form a keratosis plug
- Peripheral pigmentation
- Central decolorization
- Mild atrophy
- Atrophic scars may form

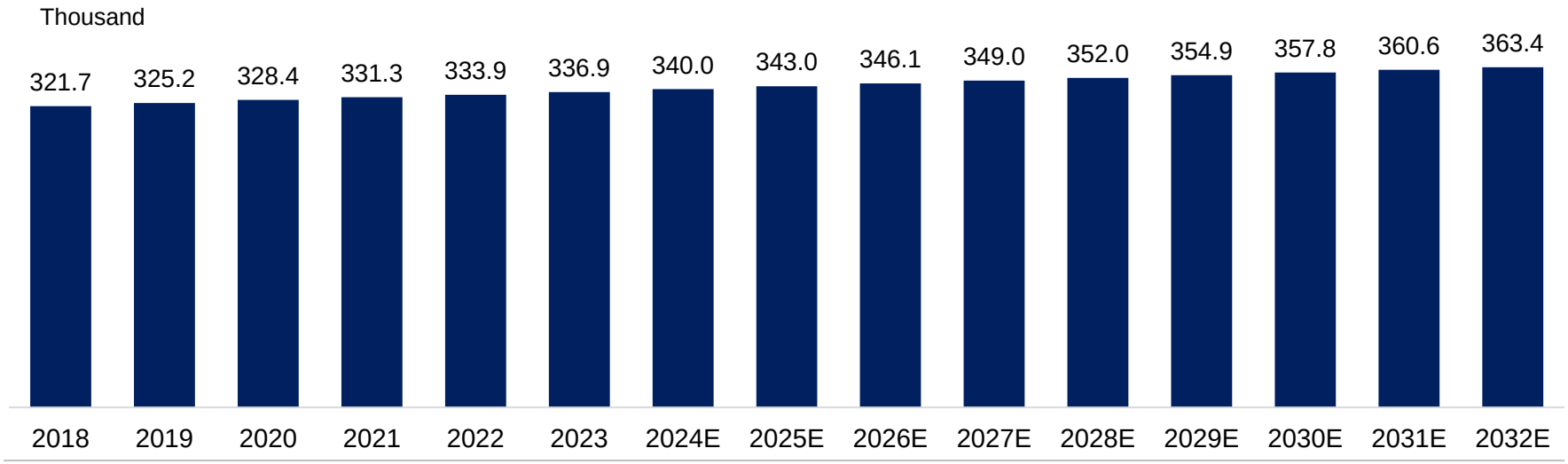
Source: Literature Review, Frost & Sullivan Analysis

Incidence of CLE in Global, 2018-2032E

- The incidence of CLE grew globally from 321.7 thousand cases in 2018 to 336.9 thousand cases in 2023 with a CAGR of 0.9%. It is predicted to increase at a CAGR of 0.9% to 352.0 thousand cases by 2028. The number of cases is then expected to increase further, with a 0.8% CAGR, to 363.4 thousand cases by 2032.

Incidence of CLE in Global, 2018-2032E

	CAGR
2018-2023	0.9%
2023-2028E	0.9%
2028E-2032E	0.8%



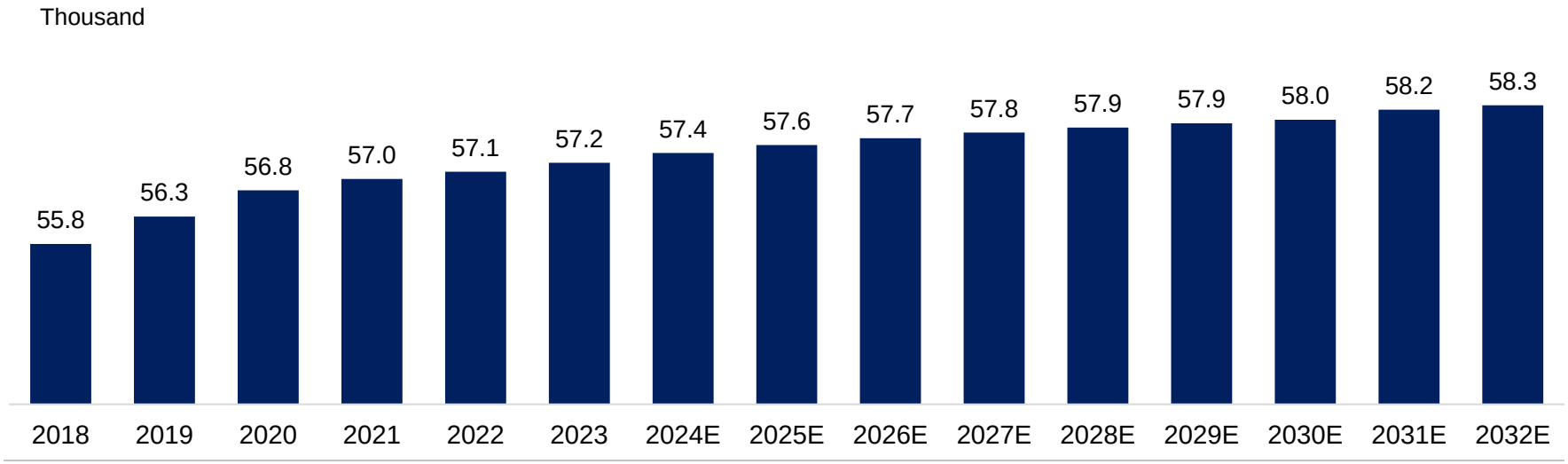
Source: Frost & Sullivan analysis

Incidence of CLE in China, 2018-2032E

- The incidence of CLE grew in China from 55.8 thousand cases in 2018 to 57.2 thousand cases in 2023 with a CAGR of 0.5%. It is predicted to increase at a CAGR of 0.2% to 57.9 thousand cases by 2028. The number of cases is then expected to increase further, with a 0.2% CAGR, to 58.3 thousand cases by 2032.

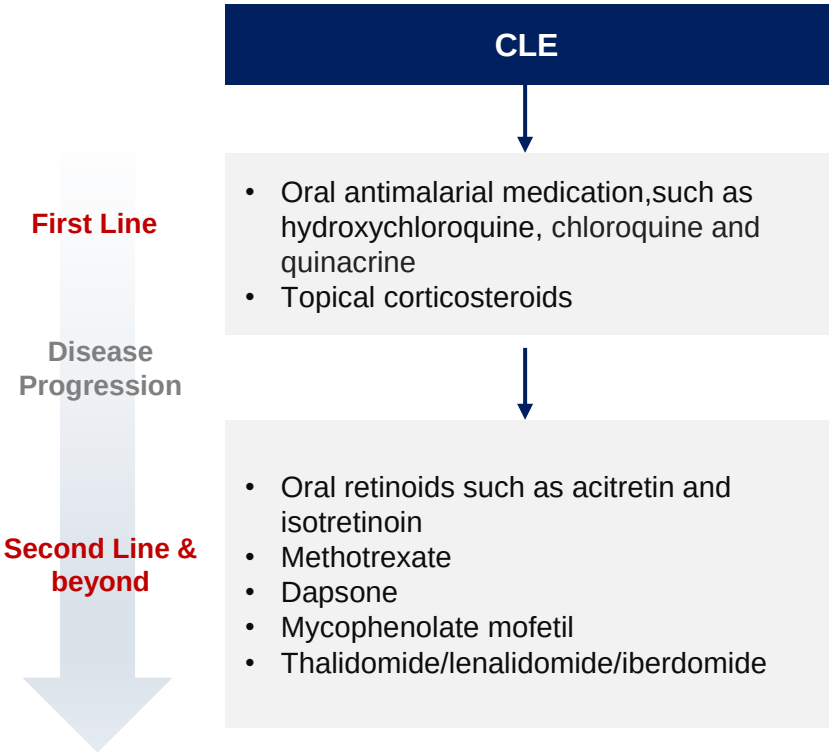
Incidence of CLE in China, 2018-2032E

	CAGR
2018-2023	0.5%
2023-2028E	0.2%
2028E-2032E	0.2%



Source: Frost & Sullivan analysis

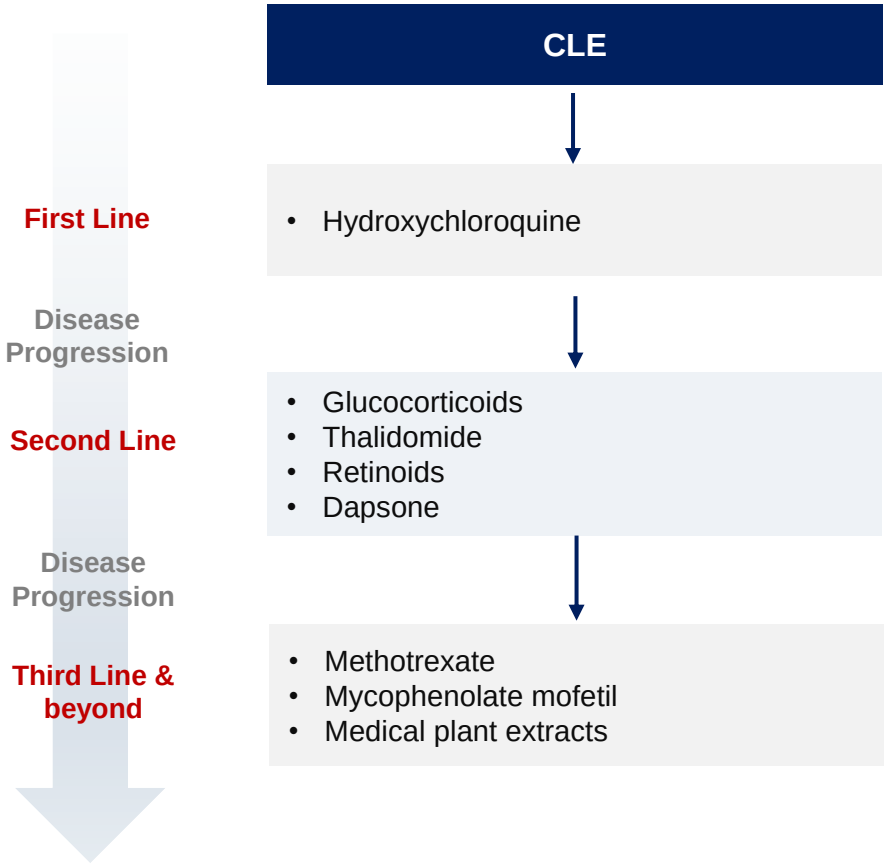
Treatment Paradigm of CLE in U.S.



Notes:. DB-2304 is indicated for CLE patients.

Source: An update on the management of refractory cutaneous lupus erythematosus, Frost & Sullivan Analysis

Treatment Paradigm of CLE in China



Notes:. DB-2304 is indicated for CLE patients.

Source: Treatment Guidelines for Cutaneous Lupus Erythematosus, Frost & Sullivan Analysis

Appendix for Verification – IO section

- The treatment landscape of major diseases, such as cancer and autoimmune diseases, has undergone a dynamic transformation. For decades, systemic treatments, such as chemotherapy and radiotherapy, have been the mainstays in the standard of care for cancer and other diseases. While these treatments can be applied to a broad spectrum of cancer types, their indiscriminate nature can damage healthy cells and often causes serious side effects, prompting the revolutionary development of precision treatments and immunotherapies for cancer in recent years. Immunotherapies, such as PD-(L)1 checkpoint inhibitors, have transformed the treatment landscape for cancer with improved efficacy and better tolerability. However, these treatments still face significant limitations, including a large population of unresponsive or resistant patients and treatment discontinuation due to side effects.
- ADCs have emerged as one of the most promising and fastest-growing treatment modalities, with the ability to leverage the targeting and binding abilities of antibodies to precisely deliver cytotoxic payloads to cancer or other diseased cells. The first ADC was approved in 2000, and 11 of the 16 marketed ADCs to date were approved after 2019, with five ADCs achieving blockbuster status (i.e., more than US$1.0 billion in annual sales).
- Building upon earlier technologies and successes, ADCs have reached an inflection point with their full potential ready to be unleashed. Substantial research is being conducted to optimize each component of the ADC— the payload, linker and antibody–exploring new formats, targets and mechanisms. These efforts aim to improve efficacy and safety of ADCs to advance the modality towards first-line treatment and establish a new standard of care. Beyond oncology, ADCs is a promising modality in other underserved therapeutic areas, such as autoimmune, metabolic and cardiovascular diseases. These ongoing advancements are propelling ADCs to explore new frontiers, unlocking the promise of this innovative modality to benefit a much wider patient population.
- ADCs have attracted significant interest and investment in the pharmaceutical industry. Each of the global top-ten MNCs has established an ADC presence, through in-house development or external collaboration and investment. Since [2022], the ADC industry has witnessed a record-breaking volume of over [20] [licensing] deals by global MNCs in aggregate, with a total deal value of over US$[60] billion.
- Notably, China-based biopharmaceutical companies have emerged as dominant players. As the licensors in a majority of these deals, China-based companies have exemplified strong ADC discovery and development capabilities. Since [2022], over [20] ADC assets have been [licensed or acquired] for a total deal value of over US$[35] billion from China-based companies. [China-based companies and institutions] also ranked second in the world in terms of the number of ADC-related journal articles published and the number of patents granted in[2022]. China's leading position is attributed to its robust interdisciplinary R&D capabilities. In addition, the innovation-oriented regulatory framework, including expedited approval process, incentives to innovative R&D and promotion of international collaboration, also support innovation and accelerate drug development in China.

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- As “guided missiles,” ADCs combine the target selectivity of antibodies and the cancer-killing potency of cytotoxic drugs. This synergistic design potentially reduces off-target, systemic toxicity and allows the targeted delivery of highly potent cytotoxic drugs that would otherwise be intolerable in systemic therapies such as chemotherapies, thereby leading to a wider therapeutic window, improved efficacy, duration of response and overall survival in cancer patients. Notably, the achievement of bystander killing effects by topoisomerase-based ADCs in recent years have further enhanced efficacy by enabling killing of neighboring tumor cells that may not express the target antigen.
- Despite their vast therapeutic potential, early generations of ADCs faced various challenges, including intolerable toxicity and suboptimal efficacy that stymied numerous ADC development programs from the 1980s to the 2000s. The first ADC, Mylotarg , was approved by the United States Food and Drug Administration (“FDA”) in 2000 for the treatment of acute myeloid leukemia. Since then, ADC technology has undergone continuous innovation, bringing substantial improvements in stability, tolerability and efficacy. Examples include the introduction of bystander killing effects through new payloads with better cross-cell permeability, the evolution from chimeric antibodies to humanized antibodies, cleavable linkers for payload release in the tumor microenvironment, and advancements in site-specific conjugation techniques to improve therapeutic window. These technological breakthroughs have expanded the application of ADCs from blood cancers only to a growing number of solid tumors. Significant efforts are being made to investigate new and emerging targets with nonapproved drugs, such as B7-H3 and HER3. There are also continuous efforts to optimize each of the three ADC components for difficult-to-treat tumors with low or ultralow protein expression, such as HER2-low breast cancer (“BC”) and endometrial cancer (“EC”).
- The next wave ADCs are expected to leverage novel linkers and payloads, moving beyond traditional cytotoxic agents to employ innovative molecules such as immunomodulatory payloads. Other innovation fronts in ADCs include the exploration of novel bispecific and multi-specific formats, and potential combination therapies with other treatment modalities to create synergistic effect. All these advancements will pave the way for ADCs to expand towards earlier lines of treatment and beyond oncology.
- Payload design is a crucial factor to the success of an ADC drug, and involves selecting a cytotoxic agent with the optimal potency and a mechanism of action suitable for the target tumor type. A well-designed payload typically possesses a small molecular weight to enable good tissue penetration, coupled with a short half-life to reduce systemic exposure and potential off-target toxicity, while maintaining a sufficient concentration within the tumor microenvironment to exert the desired cytotoxic effects. Payload design has been a key focus in ADC innovation with significant improvements over the years. While traditional payloads such as monomethyl auristatin E (“MMAE”) have their advantages, topoisomerase-based inhibitors have revolutionized the ADC modality, with their ability to exert bystander killing, high potency, effective mechanism of action and accessibility for linker attachment.

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- Antibody requires careful consideration of the target antigen's expression profile, internalization rate, and potential for off-target toxicity, where the chosen antibody possesses the desired specificity and affinity to ensure efficient and targeted delivery of the payload to the tumor cells. However, challenges remain in identifying suitable antigens with limited expression in healthy tissues, developing antibodies with optimal pharmacokinetic and pharmacodynamic properties, and mitigating potential immunogenicity of the antibody. In addition, new targeting backbones, such as bispecific antibodies, are being developed to achieve synergistic anti-tumor effects and increase tumor specificity. The complexity of combining targets with different targeting moieties introduces new challenges in antibody selection and engineering.
- Linker design focuses on selecting a linker that is stable in circulation to minimize premature payload release and systemic toxicity, while also enabling efficient release of the active drug within the target cells and tissues. Linkers can be broadly categorized into cleavable and non-cleavable linkers, chosen based on payload properties and the desired release mechanism. For example, cleavable linkers can achieve more targeted and precise delivery through their controlled release mechanism, whereas non-cleavable linkers are typically more stable in circulation. Other linker design considerations include ensuring consistent drug-to-antibody ratio ("DAR") through site-specific conjugation, and minimizing the impact of the linker on the ADC's pharmacokinetics and immunogenicity.
- The global ADC market has witnessed rapid growth in recent years following the approval of novel ADCs that demonstrate enhanced safety and efficacy profiles. For example, Padcev®, a Nectin-4 targeted ADC, and Enhertu®, a HER2-targeted ADC, both of which received initial FDA approval in 2019, have experienced rapid uptake and commercial success in recent years. In 2023, Padcev® and Enhertu® generated [global sales revenue of US$[1,178.0] million and US$[2,566.0] million, respectively.
- The U.S. and China are expected to remain the largest and fastest-growing markets for ADCs, with a CAGR of 30.9% and 72.6% from 2023 to 2028, respectively. In addition, with the exploration of this modality in non-oncology indications, ADCs for autoimmune diseases are expected to further enlarge the ADC market.

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- Broadened application through technology advances. Significant investments are being devoted to cancer research and drug development, with the goal to further elucidate disease biology and discover targeted cancer treatments that improve patient outcomes. In particular, ongoing ADC research and development on novel payloads can potentially yield new designs that improve the therapeutic effects of this modality and reduce toxicity that limits the use of some marketed ADCs. To date, there are over 100 ADC candidates under clinical development globally targeting new indications not covered by approved ADCs. These efforts will drive ADCs towards becoming a backbone cancer therapy and their expansion into other therapeutic areas.
- Dynamic collaboration among market players. There has been a surge of collaboration and licensing deals in the ADC industry, with large MNCs increasing investments into this field and smaller biotechnology companies contributing significantly to the R&D of ADC candidates. Biotechnology companies often leverage their innovative capabilities and expertise to conduct initial exploratory work and proof-of-concept studies, while collaborating with MNCs provides substantial technical, financial and regulatory support to expedite further development and commercialization of promising ADC candidates. This synergistic collaboration model has been instrumental in bringing novel candidates to the market.
- Cancer is the leading cause of mortality worldwide, resulting in approximately [10] million deaths globally [each year].In line with the continuous growth of cancer incidence, the global cancer drug markets have expanded rapidly in recent years. Despite the advancement of various cancer treatment modalities in recent years, there remains a substantial unmet need for novel, differentiated therapies that can enhance the overall survival of cancer patients. These unmet needs have grown even more pressing as the patient population continues to expand.
- HER2 is a cell surface receptor protein within the HER family that plays a key role in regulating cellular growth, division and survival. Upon activation by ligand binding or overexpression, HER2 dimerizes with other HER family members, leading to the activation of downstream signaling cascades such as the PI3K/AKT and MAPK/ERK pathways. These pathways promote cell proliferation, inhibit apoptosis, and enhance cell migration and invasion. HER2 is lowly expressed in normal tissues, but its aberrant activation through overexpression in tumor cells promote their growth and survival, thus driving the development of various types of cancers. HER2 has become a well-established cancer drug target with successful HER2-targeted therapies in different modalities, among which HER2 ADC represents one of the most successful strategies.

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- The first ADC targeting HER2 in the world, Kadcyla®, was approved [in 2013].
- BC is the second largest cancer type in the world with incidence of approximately 2,408.0thousand cases globally and 365.1 thousand cases in China in 2023. HER2 is expressed in approximately 70% of BC cases, with expression levels varying from high (IHC 3+ or IHC2+/ISH+) to low (IHC 2+/ISH- or IHC 1+).
- As of the Latest Practicable Date, only one HER2 ADC, Enhertu®, was approved for HER2-low BC and only for patients who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within six months of completing adjuvant chemotherapy, highlighting a significant unmet need among the large HER2-low or null patient population.
- HER2-low BC is the most prevalent subtype of BC, accounting for approximately [50]% of total BC cases.
- The current treatment paradigm for EC has significant limitations. ETs, such as aromatase inhibitors and a selective estrogen receptor degrader represent the cornerstone of standard 1L and 2L treatment options for advanced HER2-low BC in China and the U.S. However, the recurrence rate after using endocrine therapy is approximately 40-50%. Limited effective treatment options are available for those recurrent patients, leaving a need for effective non-endocrine therapy-based treatment.
- HER2+ BC is an aggressive type of BC, representing approximately 15-30% of total BC cases. Up to 10% of HER2+ BC patients present with metastatic disease at the time of diagnosis, and approximately 20% of patients will develop distant metastases after the primary treatment of early-stage disease.
- With the approval of effective treatments such as HER2 ADCs in recent years, HER2+ BC patients have experienced increased progression free survival (“PFS”) and overall survival (“OS”). However, there is still a risk of acquired resistance and need for safer treatments for long-term use. Approved HER2 ADCs, Kadcyla®, for example, carry black box warning issued by the FDA for hepatic, cardiac and embryo-fetal toxicities, indicating the need for future improvements in safety profiles of HER2 ADCs.

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- In China, for HR+/HER2-low BC patients who have not undergone CDK4/6 inhibitor treatment, endocrine therapies (“ETs”) with CDK4/6 inhibitor are recommended as level I treatment option. For patients with prior CDK4/6 inhibitor treatment, trastuzumab deruxtecan (Enhertu®, HER2 ADC), chemotherapy and other ET-based therapies are recommended as level II treatment options. Sacituzumab govitecan (Trodelvy®, TROP2 ADC) is recommended as level III treatment. For HR-/HER2-low BC patients, chemotherapy with or without immunotherapy is recommended as first-line treatment. ADCs such as trastuzumab deruxtecan (Enhertu®, HER2 ADC) or sacituzumab govitecan (Trodelvy®, TROP2 ADC) are recommended as the first choice of subsequent treatment.
- In the U.S., for HR+/HER2-low BC patients, ET-based therapy with CDK4/6 inhibitors is recommended as 1L treatment. 2L treatment include targeted therapies such as alpelisib, olaparib and talazoparib, and estrogen receptor degrader such as elacestrant, which are recommended according to driver mutations status. Chemotherapy is also used in 2L+ settings for patients with imminent organ failure or rapid progressive disease. Trastuzumab deruxtecan (Enhertu®, HER2 ADC) and sacituzumab govitecan (Trodelvy®, TROP2 ADC) are used in 3L+ settings. For HR-/HER2-low BC patients, chemotherapy with or without pembrolizumab can be considered as first-line treatment. Trastuzumab deruxtecan (Enhertu®, HER2 ADC) and sacituzumab govitecan (Trodelvy®, TROP2 ADC) are recommended to be used in the second-line setting and beyond.
- In China, for trastuzumab-sensitive patients, level I recommended treatments include (i) combination therapy of docetaxel, trastuzumab and pertuzumab, (ii) combination therapy of docetaxel and trastuzumab plus pyrotinib. Level II recommended treatments include (i) combination therapy of docetaxel, capecitabine and trastuzumab, and (ii) trastuzumab with chemotherapy. Level III recommended treatments include (i) pyrotinib plus capecitabine, and (ii) combination therapy of trastuzumab and pertuzumab plus chemotherapy. For trastuzumab ® resistant patients, trastuzumab deruxtecan (Enhertu®, HER2 ADC) is recommended as a level ® I treatment option, and trastuzumab emtansine (Kadcyla®, HER2 ADC) as a level II treatment option. For TKI-resistant patients, trastuzumab deruxtecan and trastuzumab emtansine are also recommended as level II treatment options.
- In the U.S., for recurrent unresectable HER2+ BC eligible for HER2 mAb treatment, 1L treatments comprise taxane-based chemotherapy in combination with pertuzumab and trastuzumab (HER2 mAbs) and 2L options include trastuzumab deruxtecan. Combination therapies such as tucatinib and trastuzumab plus capecitabine, and trastuzumab emtansine (Kadcyla®, HER2 ADC) are recommended in 3L+ settings.
- In China and the U.S., for limited stage SCLC patients, chemotherapy involving etoposide plus cisplatin with concurrent radiotherapy is recommended as 1L treatment.

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- Endometrial cancer is one of the most common gynecological cancers in the world. As one of the fastest growing cancers in terms of incidence, new cases of EC increased from 343.9 thousand in 2018 to 401.7 thousand in 2023 and is projected to reach 494.1 thousand in 2032. While EC has traditionally been more prevalent in post-menopausal women, there is a growing incidence in younger women, indicating increasing medical needs.
- In China, first-line systemic therapy for recurrent and metastatic EC use carboplatin with paclitaxel as level I recommended treatment. Level II treatment options include (i) combination therapies of carboplatin with paclitaxel plus trastuzumab or bevacizumab, and (ii) combination therapy of carboplatin with docetaxel. In 2L setting, level I recommended treatment options include (i) pembrolizumab or lenvatinib, and (ii) immunotherapy such as dostarlimab (PD-(L)1 inhibitor).
- In the U.S., first-line treatment options for recurrent disease include (i) combination therapy of carboplatin and paclitaxel with or without pembrolizumab or dostarlimab, (ii) combination therapy of carboplatin and paclitaxel with or without trastuzumab for HER2+ patients. 2L treatment options include (i) combination therapy of cisplatin and doxorubicin with or without paclitaxel, (ii) combination therapy of cisplatin with gemcitabine, (iii) monotherapy of cisplatin, carboplatin or doxorubicin and others.
- The current treatment paradigm for EC has significant limitations. For patients not suitable for total hysterectomy, traditional drug treatments have substantial side effects. In addition, a significant percentage of patients develop advanced and recurrent disease after first-line treatment, and have limited response to second- or third-line treatment. Immunotherapy has shown some promise, but its efficacy for a wider group of patients is yet to be validated, leaving vast potential for future improvements in therapies for ECs.
- As of the Latest Practicable Date, no HER2 ADC had been approved for EC across HER2- expression levels globally, and DB-1303 was the only HER2 ADC candidate in phase 3 clinical development or beyond for EC patients across HER2 expression levels.
- As of the Latest Practicable Date, there were two HER2 ADCs approved in the U.S., namely Enhertu® and Kadcyla®, and one additional in China, Aidixi ®. As of the same date, there were three HER2 ADCs (including Enhertu®) in phase 3 clinical development or beyond under global multi-regional clinical trials (“MRCTs”). The following tables illustrate the competitive landscape of marketed HER2 ADCs and HER2 ADC in phase 3 clinical development or beyond..
- B7-H3 is a prominent member of the B7 family that plays a critical role in promoting tumor progression and metastasis. B7-H3 can effectively inhibit the function of T cells and NK cells, and inhibit the production of cytokines, thus possibly promoting the immune escape of cancer cells. High expression of B7-H3 is widely observed in various solid tumors, including lung cancer, BC and prostate cancer. B7-H3 is an active area of research and a potential therapeutic target for its role in tumor immune evasion, making it a potential backbone treatment target for multiple cancer types.

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- As of the Latest Practicable Date, no B7-H3-targeting drug had been approved globally. Clinical development has been conducted to develop therapies leveraging B7-H3's role in inhibiting tumor growth and enhancing anti-tumor immunity in various cancers.
- Lung cancer is the most common cancer and the leading cause of cancer death worldwide. Small-cell lung cancer ("SCLC") represents 10-15% of all lung cancer cases [globally].The global incidence of SCLC increased from 332.9 thousand cases in 2018 to 382.8 thousand cases in 2023, and is projected to reach 484.1 thousand cases by 2032. In China, incidence of SCLC increased from 142.7 thousand cases in 2018 to 163.5 thousand cases in 2023, and is projected to reach 202.1 thousand cases by 2032. SCLC has two stages: limited stage, which is confined to one side of the chest, and extensive stage, which spreads beyond the chest to other body parts. As a highly aggressive cancer, the average five-year survival rate for SCLC patients in extensive stage is less than 5%.
- For extensive stage SCLC patients in China, level I recommendations for those without local symptoms and brain metastasis include chemotherapy such as etoposide and carboplatin used with or without immunotherapies such as serplulimab, adebrelimab, atezolizumab and durvalumab (PD-(L)-1 inhibitors). For patients with local symptoms, level I recommendations consist of radiotherapy with chemotherapy. For patients with brain metastasis, level I recommendations consist of immunotherapies such as atezolizumab (PD-1 ligand 1 ("PD-L1") inhibitor) used in combination with chemotherapy regimens involving etoposide and carboplatin, and whole brain radiotherapy. In 2L+ settings, topotecan, irinotecan and clinical trials enrollment are recommended.
- For extensive stage SCLC patients in the U.S., preferred treatment options include (i) chemotherapy of etoposide plus carboplatin, used in combination with atezolizumab and durvalumab (PD-(L)1 inhibitors), and (ii) chemotherapy of etoposide plus cisplatin, used in combination with durvalumab (PD-(L)1 inhibitor). Other recommended regimens include doublet chemotherapy etoposide with carboplatin or cisplatin. Subsequent lines of treatments include (i) platinum-based doublet chemotherapy, (ii) topotecan-based and taxane-based chemotherapy and other monotherapy such as lurbinectedin, and (iii) immunotherapies such as nivolumab and pembrolizumab (PD-1 inhibitors).
- While chemotherapy is still the mainstay for SCLC treatment, SCLC patients often develop resistance to chemotherapy and the disease often relapses within one year. Relapsed SCLC patients often have worse prognosis, with limited treatment options available. While immunotherapies such as PD-(L)1 inhibitors are also recommended in frontline settings for extensive stage SCLC patients, there remains a significant unmet need for new and more effective treatments for SCLC patients. B7-H3 overexpression is reported in 65% of all SCLC cases, making a promising target for novel treatments of SCLC.
- CRPC is a severe form of prostate cancer that exhibits resistance to treatments aiming to reduce testosterone levels. Among the subtypes of CRPCs, metastatic CRPC ("mCRPC") is a particularly advanced and challenging type.

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- Among the subtypes of CRPC, metastatic CRPC (“mCRPC”) is particularly advanced and challenging.
- In China, for mCRPC patients without prior treatment of androgen deprivation therapy (“ADT”) and chemotherapy, level I recommended treatment options include (i) abiraterone or prednisone, (ii) olaparib plus abiraterone, (iii) enzalutamide, and (iv) docetaxel. For patients with ADT failure and without prior treatment of chemotherapy, docetaxel or olaparib is recommended as level I treatment. For patients with docetaxel treatment failure and without prior treatment of ADT, abiraterone, prednisone, enzalutamide or olaparib is recommended as level I treatment. For patients with docetaxel treatment failure and with prior treatment of chemotherapy, olaparib is recommended as level I treatment. Radium-223 is also recommended for patients with symptomatic bone metastases.
- In the U.S., preferred regimens for mCRPC patients without prior docetaxel and novel hormone therapy consist of abiraterone, docetaxel and enzalutamide. For patients with disease progression after prior novel hormone therapy without prior docetaxel, preferred regimens consist of (i) docetaxel and (ii) olaparib or rucaparib. For patients with disease progression after prior docetaxel without prior novel hormone therapy, preferred regimens consist of abiraterone, cabazitaxel and enzalutamide. For patients with disease progression after prior docetaxel and novel hormone therapy, preferred regimens consist of cabazitaxel and docetaxel rechallenge. Other regimes include radium-223, niraparib,and pembrolizumab, recommended based on metastases and mutation status.
- The current treatment paradigm for mCRPC remains limited in its ability to provide durable and effective long-term control. Drug resistance remains a critical challenge in the treatment of mCRPC. While androgen deprivation therapy (“ADT”) like enzalutamide and abiraterone provides initial benefits, most patients eventually develop resistance, leading to disease progression, underscoring the potential of innovative targeted therapy to address this unmet need. With a B7-H3 expression rate as high as 93% in all CRPC cases, B7-H3 ADCs are a promising treatment option for CRPC.
- As of the Latest Practicable Date, there were no approved B7-H3 drugs, including ADCs, globally. As of the same date, there were five B7-H3 ADC candidates under global MRCTs. The following tables illustrate the global competitive landscape of B7-H3 ADC candidates under clinical development.
- HER3 is a cell surface receptor that is a member of the HER family, playing crucial roles in tumor survival and growth. In contrast to other HER family members, HER3 is not oncogenic when overexpressed alone. However, ubiquitous HER3 expression is detected in various solid tumors, including breast, lung, colorectal, prostate, and head and neck cancers.
- Despite lacking intrinsic tyrosine kinase activity, HER3 is activated by dimerization with another receptor, with EGFR and HER2 being its preferred dimerization partners, ultimately promoting tumorigenesis, metastatic dissemination and drug resistance. Moreover, therapies targeting HER3 can mediate resistance to targeted therapy, including resistance of NSCLC patients to EGFR targeted therapy.

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- Despite the growing research and clinical interest in HER3, its exploration is still limited and development of HER3-targeted drugs have been challenging due to the limited understanding of its complex signaling pathway, its lack of intrinsic kinase activity and limited internalization. As of the Latest Practicable Date, there were no approved HER3-targeting drugs globally. HER3 ADCs present significant potential with highly potent cytotoxic payloads that bypass the need for strong intrinsic kinase activity, the ability to conduct bystander killing and improved antibody engineering to enhance internalization. The features of ADCs and characteristics of HER3 biology make HER3 ADCs a promising all-comer drug.
- NSCLC is the most common subtype of lung cancer and represents approximately 85% of all lung cancer cases globally..
- A set of genetic abnormalities occurring in NSCLC have been identified as predictors for patients' responses to various targeted therapies, including EGFR mutations. Treatments developed specifically for different subtypes of NSCLC based on these genetic differences can be more effective for disease control.
- EGFR-mutant ("EGFRm") NSCLC is a prevalent subtype of NSCLC with approximately 700 thousand new cases each year globally. EGFR mutations are particularly prevalent in Asian population, accounting for over 50% of all NSCLC cases in this demographic group.
- In China, the 1L treatment for EGFRm NSCLC patients include (i) TKIs, such as osimertinib, almonertinib, fumatinib, befotertinib, afatinib, dacomitinib, gefitinib, erlotinib, and icotinib, (ii) combination therapy of TKIs and mAbs, (iii) platinum-based doublet chemotherapy plus bevacizumab and (iv) combination therapy of TKIs and chemotherapy. Second and subsequent lines of treatments include (i) continuous original EGFR-TKI treatment in combination with local treatment, (ii) single-agent chemotherapy and (iii) anlotinib. In the U.S., the 1L treatment for EGFRm NSCLC patients include (i) TKIs, such as afatinib, erlotinib, dacomitinib, gefitinib and osimertinib, (ii) combination therapy of TKIs and mAbs, such as erlotinib with ramucirumab or bevacizumab. In 2L+ settings, TKIs such as osimertinib and mobocertinib, and bispecific antibodies ("bsAbs") such as amivantamab are recommended.
- TKIs are still the mainstay for EGFRm NSCLC treatment. However, most patients eventually acquire resistance with median relapse occurring approximately [9-14 months] after treatment with TKIs. For patients who have failed TKIs, effective treatment options are limited. HER3 has become a validated target for EGFRm NSCLC, supported by promising efficacy data shown in several pivotal trials. EGFR and HER3 can together form heterodimeric complexes, leading to the activation of downstream signaling pathways. HER3 is also shown to be an escape mechanism involved in resistance to EGFR TKI therapies.

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- HER3 is expressed in approximately 90% of prostate cancer cases and is commonly overexpressed, making it an actionable target in treating prostate cancer, including CRPC. The current treatment paradigm for CRPC remains limited in its ability to provide durable and effective long-term control, underscoring the potential of innovative targeted therapy to address this unmet need.
- As of the Latest Practicable Date, there were no approved HER3-targeted therapies, including ADCs, globally. As of the same date, there were four HER3 ADC candidates under global MRCTs and three other HER3 ADC candidates under clinical development. The following table illustrates the global competitive landscape of HER3 ADC candidates under clinical development.
- TROP2 is a transmembrane protein that has essential functions in embryonic and organ development with low expression in normal tissues. TROP2 is a clinically valuable ADC target as it is overexpressed with low heterogeneity in a wide range of highly prevalent or hard-to-treat cancers, including advanced tumors with limited actionable targets.
- TROP2 ADCs have also demonstrated synergistic anti-tumor activity in various preclinical and clinical studies as the backbone of potential combination therapies with other treatment modalities such as chemotherapy, targeted therapy and immunotherapy.
- Despite the encouraging therapeutic benefits shown by TROP2 ADCs, the global clinical development of TROP2 ADCs is currently heavily focused in TNBC, HR+/HER2- BC, UC and NSCLC. This leaves significant unmet needs among patients with other prevalent or hard-to-treat cancers, such as ovarian cancer (“OC”).
- [OC is the third most common cancer of the female reproductive system worldwide.]
- In China, 1L treatments for OC include (i) carboplatin and paclitaxel or docetaxel or doxorubicin liposome, (ii) paclitaxel and carboplatin with bevacizumab. For relapsed patients resistant to platinum-based chemotherapy, recommended treatments include (i) doxorubicin liposome with or without bevacizumab, (ii) docetaxel or etoposide or gemcitabine, (iii) topotecan hydrochloride with or without bevacizumab, (iv) doxorubicin liposome plus apatinib, and (v) PARP inhibitors.
- In the U.S., preferred regimens for primary therapy of OC include (i) carboplatin and paclitaxel, (ii) 5-FU, leucovorin and oxaliplatin, (iii) capecitabine and oxaliplatin, and (iv) hormone therapy such as anastrozole, letrozole and exemestane. For platinum-sensitive patients, recurrence therapy include (i) carboplatin and gemcitabine with or without bevacizumab, (ii) carboplatin and doxorubicin liposome with or without bevacizumab, (iii) carboplatin and paclitaxel with or without bevacizumab, and (iv) cisplatin and gemcitabine. For platinum-resistant patients, preferred regimens include (i) cyclophosphamide or bevacizumab, (ii) docetaxel, (iii) etoposide, (iv) gemcitabine, and (v) liposomal doxorubicin or paclitaxel or topotecan with or without bevacizumab.

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- Chemotherapy represents the mainstay of standard treatments for advanced OC in China and the U.S., which involves platinum-based and taxane-based chemotherapy with or without antiangiogenic mAb bevacizumab. However, the disease often recurs in a more resistant form even after initial successful treatment with surgery and chemotherapy. Immunotherapy, such as PD-1 inhibitors may be considered for patients with certain immunotherapy biomarkers who have no satisfactory alternative treatment options. However, immunotherapies, while promising, has shown limited effectiveness in OC when used as a monotherapy. This limited efficacy and high recurrence rate underscores the need for more effective and durable treatment options that can improve long-term survival outcomes for patients.
- Traditionally, ADC development has focused on FR-positive OC patients, who constitute a limited subset of the OC population. Given that TROP2 is overexpressed in the majority of OC patients and the under-exploration of OC as an indication for other TROP2 ADC candidates, TROP2 ADCs targeting OC patients represent a promising therapeutic strategy with vast potential. In addition, TROP2 ADCs can potentially bypass platinum resistance, providing a novel therapeutic option when standard platinum-based chemotherapy is no longer effective. They can also be used in combination with or as a complement to standard platinum-based chemotherapy, potentially enhancing treatment efficacy..
- TROP2 is broadly overexpressed in NSCLC, making TROP2 ADCs a promising modality for treating advanced NSCLC regardless of driver mutation status. Lung cancer is the most common cancer and the leading cause of cancer death worldwide, with NSCLC accounting for over 85% of all lung cancer cases.
- As of the Latest Practicable date, Trodelvy was the only TROP2-targeted drug approvedboth in the U.S. and in China, indicated for mTNBC, metastatic UC (“mUC") and HR+/HER2BC in the U.S., and for mTNBC in China. Despite its promising clinical activity, Trodelvy is associated with severe neutropenia (i.e., a lower-than-normal number of neutrophils in theblood) and severe diarrhea, two serious adverse reactions for which Trodelvy has black box warnings issued by the FDA. Consequently, there is a need for novel TROP2 ADCs that havelimited toxicities while maintaining robust anti-tumor activity, As of the same date, there were one additional TROP2-targeted drug approved in China, SKB264 (brand name: 佳泰莱”)indicated for mTNBC, and one approved in the U.S., Datroway, indicated for HR+/HER2 BC.
- BsADCs are next-generation therapeutics that combine the targeting precision of bsAbs with the potent cytotoxicity of ADCs. By incorporating two distinct binding sites in a single therapeutic entity, BsADCs can potentially offer meaningful advantages over traditional monospecific ADCs and their combination therapies. While promising, the complexity of BsADCs introduces new challenges in antibody engineering, stability and manufacturing, setting a high entry barrier.

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- BsADCs employ various design strategies to enhance therapeutic efficacy and safety, represented by the tumor-associated antigen ("TAA") + immunotherapy ("IO") approach and the dual-TAA approach. The TAA + IO strategy utilizes dual-function antibodies that simultaneously target TAA on cancer cells to induce direct tumor cell death while engaging IO targets to activate the immune system, promoting more potent and durable anti-tumor responses.
- By comparison, the dual-TAA approach targets two distinct, carefully selected TAAs co-expressed on cancer cells, enhancing binding specificity, reducing off-tumor toxicity, and potentially overcoming tumor heterogeneity and antigen escape mechanisms.
- Both strategies aim to improve the therapeutic index of ADCs by increasing tumor specific targeting while minimizing off-target effects, with the choice between approaches depending on the specific cancer type, target availability, and desired mechanism of action. In recent years, BsADC as a new modality has attracted growing interest and development, with over ten BsADCs under current clinical development across a broad range of solid tumors and hematological malignancies.
- BsADCs that can simultaneously block both PD-(L)1 and B7-H3 pathways are developed under the TAA+IO approach to synergistically enhance T cell activity and cancer cell killing. B7-H3's pan-cancer expression coupled with PD-L1's immune-modulating function may offer enhanced anti-tumor effects across broad indications. Studies have shown that B7-H3xPD-L1 BsADCs have strong binding and neutralizing capabilities and can achieve better anti-tumor activity than using PD-L1 or B7-H3 antibodies alone or in combination. B7-H3xPD-L1 BsADCs have treatment potential across various solid tumors, including SCLC, hepatocellular carcinoma ("HCC"), NSCLC, melanoma, ESCC and TNBC.
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- Autoimmune diseases are caused by the abnormal functioning of the immune system, where the body's immune system mistakenly attacks its normal cells and tissues. Many autoimmune diseases are chronic conditions that require lifelong treatment. Major types of autoimmune disease include systemic lupus erythematosus ("SLE"), cutaneous lupus erythematosus ("CLE"), rheumatoid arthritis and psoriasis.

Appendix for Verification – IO section

- For decades, a considerable number of autoimmune disease patients have suffered from drug-related side effect and emerging challenges from novel therapies such as paradoxical effects of biologics [and immune-related adverse events]. Anti-inflammatory agents, such as NSAIDs, glucocorticoids and DMARDs, are commonly used treatment options for patients with autoimmune diseases, particularly during the initial stages of disease. While they are effective in alleviating pain, reducing fever and mitigating inflammatory responses, they are limited to easing symptoms instead of treating the cause of disease. Moreover, many of these anti-inflammatory agents are systemic treatments, and as a result, may globally impair the immune system with long-term use and result in serious side effects, such as increased susceptibility to infections, metabolic disturbances and cardiovascular complications.
- In recent years, targeted treatments such as biologics have been developed and marketed with better safety profiles. However, current drawbacks of biologic therapies, including paradoxical effects of biologics, side effects on normal immune functions and responses, narrow therapeutical window due to drug resistance, and poor patient compliance resulting from the inconvenience of intravenous administration, prevent wider use of current biologics as first-line medications for autoimmune diseases. [While cell therapies such as CAR-T cell therapy has emerged as a promising approach for treating certain autoimmune diseases, the B-cell depletion associated with this therapy can subsequently jeopardize the overall integrity of patients' immune systems, presenting a significant clinical challenge.]
- ADCs represent a promising new frontier and an area of growing interest for autoimmune and inflammatory conditions given their high specificity for target cells, enabling potent payloads (anti-inflammatory agents) to be delivered with minimal impact to healthy cells. As a result, ADCs may enable durable treatment response and improved patient outcomes compared to existing therapies.
- While no autoimmune ADCs have been approved, the advantages and potential of ADCs indicated for autoimmune diseases have attracted significant research interest and investment. With the continuous advancements in this field, next-generation ADCs are expected to maximize therapeutic efficacy while minimizing the risk of off-target toxicities that have hampered some earlier autoimmune ADC candidates.
- BDCA2 is a transmembrane protein uniquely expressed on the surface of plasmacytoid dendritic cells ("pDCs"). pDCs play a crucial role in the innate immune response and BDCA2 acts as an inhibitory receptor on pDCs, modulating their activation and function. Targeting BDCA2 can inhibit pDC activation and the subsequent production of type I interferons, which are known to play a key pathogenic role in various autoimmune conditions. As a result, BDCA2 has been explored as a potential therapeutic target for autoimmune and inflammatory disorders, such as systemic lupus erythematosus ("SLE") and cutaneous lupus erythematosus ("CLE").
- Systemic lupus erythematosus is an autoimmune disease characterized by the production of autoantibodies that target the body's own tissues and cells. It is the most common type of lupus, causing widespread inflammation and tissue damage in the affected organs.

Appendix for Verification – IO section

- In China, long-term use of hydroxychloroquine is the primary treatment for SLE patients without contraindications, followed by glucocorticoids. Immunosuppressive agents are used in 2L setting when combination therapy with glucocorticoids and hydroxychloroquine is ineffective. For patients who are ineffective, intolerant, or relapse after treatment with glucocorticoids and/or immunosuppressants, biologics are recommended.
- In the U.S. 1L treatment options for SLE mainly include (i) glucocorticoids, (ii) hydroxychloroquine, and (iii) non-steroidal anti-inflammatory drugs ("NSAIDs"). Azathioprine and methotrexate are recommended as 2L treatments. 3L treatments include anifrolumab, belimumab, cyclophosphamide, mycophenolate mofetil, rituximab and voclosporin.
- With advancements in diagnostic tools and treatment options, the prognosis for individuals with SLE has improved significantly over the past few decades. However, SLE remains a chronic and potentially life-threatening condition, and calls for innovative treatment options with improved efficacy. A major shortcoming of mainstay treatments for SLE, such as glucocorticoids and immunosuppressants, is their inability to address the high heterogeneity of pathogenesis in these complex diseases, which often result in limited efficacy and serious side effects, especially when used long term for chronic disease management. Given the complex and heterogeneous nature of SLE, an ideal treatment modality for SLE should be able to achieve optimal disease control and minimize long-term side effects, calling for the development of targeted therapies such as ADCs. As a validated target that is specifically expressed on pDCs, BDCA2 and its over-production of type I interferon ("IFN-I") are crucial in SLE pathogenesis, making BDCA2-targeted ADCs promising for the treatment of SLE.
- Cutaneous lupus erythematosus is an autoimmune disorder that primarily affects the skin. CLE is characterized by a range of inflammatory skin lesions and rashes that can appear on various parts of the body, including the face, scalp, arms, and trunk.
- In China, 1L systematic therapy for CLE patients is hydroxychloroquine. Glucocorticoids, thalidomide, retinoids and dapsone are used as 2L treatments. 3L treatments include methotrexate, mycophenolate mofetil. In the U.S., 1L systemic therapy for CLE patients is the use of an oral antimalarial medication. In 2L settings, oral retinoids such as acitretin and isotretinoin, immunosuppressants such as methotrexate are recommended.
- Despite the available treatment options, many patients continue to experience suboptimal disease control, highlighting the need for more effective and targeted therapies such as ADCs to improve outcomes for individuals living with this debilitating autoimmune skin condition. As a validated target that is specifically expressed on pDCs, BDCA2 and its over-production of IFN-I are crucial in CLE pathogenesis, making BDCA2-targeted ADCs promising for the treatment of CLE.
- As of the Latest Practicable Date, there was no approved BDCA2 ADC or BDCA2 ADC candidates under clinical development globally or in China.

Appendix for Verification – Business section

- Despite the current absence of approved B7-H3-targeted therapies, B7-H3 ADCs have demonstrated encouraging clinical efficacy, notably in SCLC patients, sparking substantial interest and high-profile licensing deals in the field.
- To date, there are no B7-H3 ADC candidates indicated for CRPC that have entered into phase 3 registrational trial worldwide.
- Despite the growing research and clinical interest in HER3, it remains under-explored and has faced two decades of drug development challenges due to the complexity in achieving signaling inhibition and the potential for escape pathway activation.
- Despite the growing research and clinical interest in HER3, it remains under-explored and has faced two decades of drug development challenges due to the complexity in achieving signaling inhibition and the potential for escape pathway activation.
- OC, for example, is one of the leading cause of cancer death in women globally with over 300,000 diagnosed each year.
- Traditionally, ADC development has focused on FR-positive OC patients, who constitute a limited subset of the OC population. Compared to FR-directed ADCs, DB-1305 demonstrates broader treatment potential among a wide range of OC patients, due to TROP2's high overexpression rate (~83%) in this cancer type.
- SLE and CLE are autoimmune diseases that together affect over eight million patients globally, being one of the most advanced BDCA2 ADCs in terms of development progress.
- BDCA2 is a validated target that is specifically expressed on plasmacytoid dendritic cells ("pDCs"), whose over-production of type I interferon ("IFN-I") is crucial in SLE and CLE pathogenesis. Although BDCA2-targeted mAbs have demonstrated reduced disease activity in SLE patients, their clinical efficacy is generally limited.
- The five-year survival rate for EC patients with advanced, metastatic or recurrent disease is estimated at only 18%. The global EC drug market is expected to increase from US$5.3 billion in 2023 to US$9.0 billion by 2028, representing a CAGR of 11.2%
- To date, the only approved HER2 ADC available for EC patients globally is indicated for pan-HER2+ solid tumors and hence covers only HER2+ (IHC 3+) EC, which is estimated to account for around 17-30% of the EC patient population. Beyond this small subset of patients, approximately 47-53% of EC patients are HER2 low expressing with very limited treatment options.

Appendix for Verification – Business section

- BC is known to be the second largest cancer type in the world by incidence.
- Taking into the industry practice, the phase 1 dose escalation study constituted a completed clinical trial with its main purpose aligning with the overall purpose of a conventional phase 1 trial, and therefore the completion of the phase 1 dose escalation study is equivalent to the completion of a conventional phase 1 trial.
- SCLC is an aggressive form of lung cancer characterized by rapid growth and high rates of recurrence with a five-year survival rate of less than 7%, compared to 28% for NSCLC. However, available treatments for SCLC remain limited, primarily to chemotherapy and PD-L1 inhibitors, with few targeted therapies approved globally for this indication to date.
- While patients with metastatic prostate cancer initially respond to hormone therapy, most patients progress after 18-24 months and develop mCRPC, leading to a poor prognosis. The global CRPC drug market is expected to increase from US$3.9 billion in 2023 to US$6.5 billion by 2028, representing a CAGR of 10.9%.
- OC is the third most common cancer of the female reproductive system worldwide. High expression of TROP2 is reported in about 83% of OC patients.
- Traditionally, ADC development has focused on FR-positive OC patients, who constitute a limited subset of the OC population. Given that TROP2 is overexpressed in the majority of OC patients and the under-exploration of OC as an indication for other TROP2 ADC candidates.
- BDCA2 is a unique and clinically validated receptor expressed on pDCs. When BDCA2 is engaged by mAb, it triggers an inhibitory signaling cascade that suppresses activation of pDCs and reduces IFN-I production. This negative feedback mechanism helps to control pDC activation and prevent excessive IFN-I production.
- Given the complex and heterogeneous nature of SLE, an ideal treatment modality for SLE should be able to achieve optimal disease control and minimize long-term side effects, calling for the development of targeted therapies such as ADCs. As a validated target that is specifically expressed on pDCs, BDCA2's over-production of IFN-I is crucial in SLE pathogenesis, making BDCA2-targeted ADCs promising for the treatment of SLE.

Appendix for Verification – Business section

- A major shortcoming of mainstay treatments, such as glucocorticoids and immunosuppressants, is their inability to address the high heterogeneity of pathogenesis in these complex diseases, which often result in limited efficacy and serious side effects, especially when used long term for chronic disease management.
- BsADCs are next-generation ADCs with an innovative targeting backbone.
- Long term use of glucocorticoids, for example, are commonly associated with increased risks of bone fractures, weight gain, diabetes, immune system suppression, and other chronic conditions.
- Unique coverage of KRASm NSCLC. KRAS mutations are estimated to occur in approximately 30% of NSCLC. There are currently no global registrational trials for HER3 ADC candidates specifically targeting KRASm NSCLC.
- Patients with KRASm NSCLC typically experience rapid disease progression after KRAS TKI treatments, and those who develop drug resistance face severely limited subsequent treatment options.
- Many patients with chronic autoimmune diseases, such as SLE and CLE, are currently treated with therapies that suppress the entire immune system rather than selectively modulate specific pathways involved in autoimmune diseases. This non-specific immunosuppression often lead to severe side effects.
- As of the Latest Practicable Date, there were two HER2 ADCs approved in the U.S., namely Enhertu® and Kadcyla®, and one additional in China, Aidixi ®. As of the same date, there were three HER2 ADCs (including Enhertu®) in phase 3 clinical development or beyond under global multi-regional clinical trials.
- KRAS mutations are estimated to occur in approximately 30% of NSCLC. There are currently no global registrational trials for HER3 ADC candidates specifically targeting KRASm NSCLC.
- BsADCs that target EGFR and HER3 are a representative therapy of the dual-TAA BsADC approach. EGFR is a cell surface receptor with key roles in multiple signaling pathways that promote cell proliferation and survival. Aberrant activation of EGFR, such as overexpression or mutation, is widely established as an oncogenic driver in a wide range of cancers, such as CRC, HNSCC and NSCLC. HER3 belongs to the same family as EGFR and preferentially forms heterodimers with EGFR to activate downstream oncogenic pathways. Due to target synergies, EGFRxHER3 BsADCs have demonstrated enhanced efficacy and ability to overcome resistance to EGFR-directed treatments in clinical studies. Potential indications for EGFRxHER3 BsADCs include ESCC, HNSCC, CRC, nonmelanoma skin cancer, NSCLC, gastric cancer ("**GC**"), pancreatic adenocarcinoma, nasopharyngeal cancer, bladder cancer and BC.

Appendix for Verification – Business section

- As of the Latest Practicable date, Trodelvy® was the only approved TROP2-directed drug globally or in China, indicated for metastatic TNBC ("mTNBC"), metastatic UC ("mUC") and HR+/HER2- BC in the U.S., and for mTNBC in China. As of the same date, there were eight TROP2 ADCs indicated for OC under clinical development and eight TROP2 ADCs in combination with immunotherapies in phase 1/2 clinical development or beyond.
- Many patients with chronic autoimmune diseases, such as SLE and CLE, are currently treated with therapies that suppress the entire immune system rather than selectively modulate specific pathways involved in autoimmune diseases. This non-specific immunosuppression often lead to severe side effects.
- Immune-modulating ADCs have been validated by preliminary clinical data from peers, showing better safety and efficacy profiles compared to the antibody alone.
- As of the Latest Practicable Date, there were no approved BDCA2 ADC and no BDCA2 ADC candidates indicated for SLE or CLE under clinical development globally or in China.
- Notably, ADCs have emerged as a promising upgrade to chemotherapy in cancer treatment, as they combine the specificity of antibodies with the potent cell-killing ability of cytotoxic drugs, representing a significant market opportunity.
- Topoisomerase-based payloads, such as exatecan and its derivatives, have exhibited a favorable balance between potency and off-tumor toxicity delivering strong antitumor efficacy while minimizing adverse effects on healthy tissues.

The major entry barriers for new entrants to the ADC market are set forth as follows:

- Sophisticated development process. ADC development is a challenging process involving significant uncertainties. Many ADCs have exhibited potential inpreclinical research, but failed to perform well in clinical trials, with toxicity being one of the main factors contributing to these failures. The nature of ADCs requires robust and specialized data, such as drug-to-antibody ratio, in addition to a wide range of other parameters. Such a sophisticated development process also necessitates significant capital investment and substantial financial support, which also poses challenges to new entrants to the ADC market.
- Stringent and evolving regulatory oversight. The ADC market is subject to stringent and constantly evolving regulatory oversight, with the approval process for new ADCs often characterized by its lengthiness and high expenses. Regulatory authorities such as the FDA and the NMPA closely evaluate the safety, efficacy and quality of ADCs and ADC candidates through rigorous preclinical and clinical review. The process requires substantial documentation, additional studies and regulatory communications, making ADC development and approval time_x0002_consuming and expensive for market players, especially new entrants.

Appendix for Verification

ADC design of HER2 ADCs (DB-1303, Enhertu®(DS-8201), Kadcyla® and Aidixi®)

	DB-1303	Enhertu® (DS-8201)	Kadcyla®	Aidixi®
Antibody	Trastuzumab	Trastuzumab	Trastuzumab	Disitamab
Linker	Tetrapeptide-based cleavable linker	GGFG linker	MCC linker	Val-Cit linker
Payload	P1003, an exatecan derivative and a moderately potent TOPO I inhibitor	Dxd, an exatecan derivative and a moderately potent TOPO I inhibitor	DM1, a maytansine derivative and a highly potent tubulin inhibitor	MMAE, a highly potent tubulin inhibitor
DAR	8	8	3.5	4

Source: Literature review, Frost & Sullivan

Appendix for Verification

ADC design of B7-H3 ADCs (DB-1311, DS-7300 and MGC018)

	DB-1311	DS-7300	MGC018
Antibody	Humanized anti-B7-H3 IgG1 mAb	Ifinatamab	Ifinatamab
Linker	Tetrapeptide-based cleavable linker	GGFG linker	Valine-citrulline linker
Payload	P1021, an exatecan derivative and a highly potent TOPO I inhibitor	Dxd, an exatecan derivative and a moderately potent TOPO I inhibitor	Seco-DUBA, a DNA alkylating agent
DAR	6	4	2.7

Source: Literature review, Frost & Sullivan

Appendix for Verification

ADC design of HER3 ADCs (DB-1310 and U3-1402)

	DB-1310	U3-1402
Antibody	Humanized anti-HER3 IgG1 mAb	Patritumab
Linker	Tetrapeptide-based cleavable linker	GGFG linker
Payload	P1021, an exatecan derivative and a highly potent TOPO I inhibitor	Dxd, an exatecan derivative and a moderately potent TOPO I inhibitor
DAR	8	7-8

Source: Literature review, Frost & Sullivan

Appendix for Verification

ADC design of TROP2 ADCs (DB-1305, Trodelvy®, DS-1062 and SKB264/MK-2870)

	DB-1305	Trodelvy®	DS-1062	SKB264/MK-2870
Antibody	Sacituzumab	Sacituzumab	Datopotamab	Sacituzumab
Linker	Tetrapeptide-based cleavable linker	Maleimide containing CL2A linker	GGFG linker	2-methylsulfonyl pyrimidine containing CL2A linker
Payload	P1021, an exatecan derivative and a highly potent TOPO I inhibitor	SN38, a metabolite of the camptothecin derivative and a moderately potent TOPO I inhibitor	Dxd, an exatecan derivative and a moderately potent TOPO I inhibitor	T030, a belotecan derivative TOP I inhibitor
DAR	4	7.6	4	7.4

Source: Literature review, Frost & Sullivan